New Cleroindicins from *Clerodendrum indicum*

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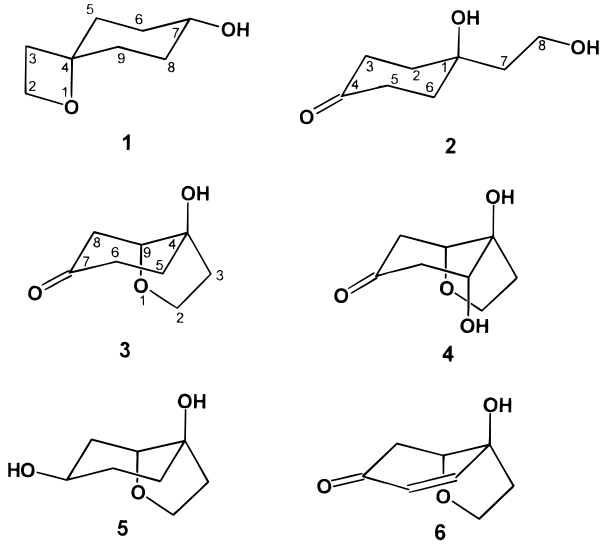
Six new compounds, cleroindicins A−F (**1**−**6**), were isolated from the aerial parts of *Clerodendrum indicum* and identified by spectral and chemical evidence. Cleroindicin A proved to be a novel spirocompound.

In our previous paper, we researched the chemical constituents of *Clerodendrum japonicum* and obtained some phenylpropanoid glycosides.[1] In a continuation of our investigations on the genus *Clerodendrum*, we studied *Clerodendrum indicum* (L.) Kuntze (Verbenaceae), which has wide distribution in the Yunnan province, China. In Dai nationality, this plant has been used to treat malaria and rheumatism.[2] This paper deals with the isolation and structure elucidation of six new compounds, named cleroindicins A−F (**1**−**6**).



Results and Discussion

An ethanolic extract of the aerial parts of *C. indicum* was fractionated as described in the Experimental Section to afford six new compounds (cleroindicins A−F, **1**−**6**).

Cleroindicin A (**1**) was obtained as white needles, mp 56−57 °C. Its molecular formula ($C_8H_{14}O_2$) was deduced from HREIMS $[M]^+$ 142.0945 (calcd 142.0994). ^{1}H-NMR and ^{13}C-NMR spectra of **1** showed that it had no double bonds or carbonyl groups; thus, it only possessed two rings based on a calculation of unsaturated degrees (n = 2). Its IR spectrum indicated the presence of hydroxy and ether linkages. The ^{13}C-NMR spectrum revealed six carbon signals: one quarternary (δ 70.3), one methine (δ 70.1), and four methylenes (δ 59.1, $-OCH_2-$; 45.4, 36.4, 31.9) were observed, suggesting that **1** was a symmetric molecule. Its ^{1}H-NMR spectrum showed seven groups of proton signals: δ 4.21 (2H, t, J = 6.6 Hz), 3.92 (1H, tt, J = 11.2, 4.1 Hz), 2.30 (2H, m), 2.08 (2H, m), 2.04 (2H, m), 2.02 (2H, t, J = 6.6 Hz), 1.54 (2H, td, J = 12.8, 3.6 Hz). The two methylenes (δ 4.21, and 2.02) only coupled with each other, indicating the presence of a $-OCH_2CH_2-$ unit. From these data, two possible structures were considered: an oxyspirane system and an oxy-bridge system. Further examination of ^{1}H−^{1}H and ^{1}H−^{13}C COSY spectra excluded the oxy-bridge structure. Both structures had symmetry of surface consistent with no optical rotation. In structure **1**, the signal (δ 3.92) due to H_{ax}-7 coupled with H-6 and H-8 split into a triple triplet (coupling constants: J_1 = 11.2 Hz, diaxial; J_2 = 4.1 Hz, axial−equatorial coupling). In the alternative structure, the dihedral angle between H_{ax}-7 and the axial protons at C-6 and C-8 was nearly equal to that between H_{ax}-7 and the equatorial protons at C-6 and C-8 due to its boatlike conformation, so that H-7 should have been simply split into a triplet with a small coupling constant according to the Karplus formula.

However, compound **1** still had two possible configurational isomers:cis and trans (**1** and a compound with inverse configuration at C-4). Determination of structure **1** began with complete assignments of the ^{1}H- and ^{13}C-NMR signals. In the ^{1}H−^{1}H COSY experiment, the proton H_{ax}-7 signal was readily recognized by its characteristic spin system [δ 3.92 (1H, tt, J = 11.2, 4.1Hz)], and it was the only methine proton on a carbon bearing one hydroxyl group. Starting from H_{ax}-7, the H_{ax}-6 and H_{ax}-8 proton signals were assigned as δ 2.30 (J = 11.2 Hz) owing to axial−axial couplings and the H_{eq}-6 and H_{eq}-8 proton signals as δ 2.04 due to axial−equatorial couplings. Similar couplings led to assignment of H_{ax}-5 and H_{ax}-9, δ 1.54 (J = 12.8 Hz). The remaining H_{eq}-5 and H_{eq}-9 protons were assigned as δ 2.08. The C-2 and C-3 protons formed an isolated spin system and were readily assigned as H-3 (δ 2.02) and H-2 (δ 4.21). On the basis of a ^{1}H−^{13}C COSY spectrum, all carbon signals were assigned: δ 59.1 (t, C-2), 45.4 (t, C-3), 70.3 (s, C-4), 70.1(d, C-7), 36.4 (2C, t, C-5, -9), 31.9 (2C, t, C-6, -8). The NOESY spectrum contained some diagnostically important correlation spots. The long-range couplings of H-3 and H_{ax}-5(9), H_{ax}-5(9), and H_{ax}-7 indicated cleroindicin A could only be structure **1**.

Acetylation of **1** using moist pyridine provided two products, which were separated into two configurational isomers **7** and **8**, as shown in Figure 1. We then repeated the reaction using dried distilled pyridine (and excess Ac_2O), and only compound **7** was obtained. Both

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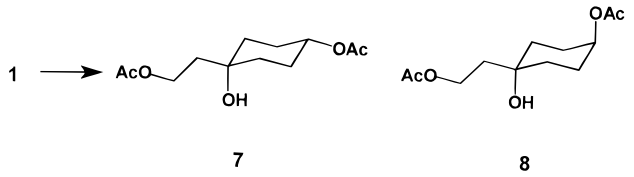

Figure 1. Acetylation of compound **1**.

7 and **8** were easily identified by NMR and EIMS methods. In compound **7**, the proton on the ring carbon bearing OAc exhibited a typical tt peak [δ 4.89 (1H, tt, J = 10.5, 3.8 Hz)] due to diaxial and axial−equatorial couplings, and it shifted downfield from δ 3.92 to 4.89 (+0.97 ppm). Similarly, H-7 (2H, t, J = 7.3 Hz) shifted downfield from δ 4.21 to 4.48 (+0.27 ppm). From the ^{13}C-NMR spectrum of **7**, the signal of C-2 shifted downfield from δ 59.1 to 61.4, while the signals C-3 and C-4 shifted upfield to δ 41.8 (−3.6 ppm) and δ 68.5 (−1.8 ppm), respectively. Moreover, the signal of C-7 shifted downfield from δ 70.1 to 72.9, while the signals of C-5 (or C-9) and C-6 (or C-8) shifted upfield to δ 35.7 (−0.7 ppm) and δ 27.5 (−4.4 ppm), respectively, by comparison with compound **1**. All these results could be explained if the four-membered oxy-spiro ring was opened and diacetylated. Compound **8** had the same molecular weight (EI-MS m/z 227 $[M + H]^+$) as compound **7**. From the ^{1}H-NMR spectrum of **8**, the proton on the ring carbon bearing OAc showed a broad singlet [δ 5.11(1H)] owing to diequatorial and axial−equatorial couplings, suggesting that it was equatorial. The remaining structure of **8** was similar to that of **7** from NMR spectral data. We presumed the following mechanisms to explain these phenomena.

In our first attempt to acetylate **1**, the existence of H_2O in pyridine made it possible for both S_N1 and S_N2 mechanisms to occur. Only the S_N2 reaction mechanism was permitted when dry pyridine was used, so compound **7** was the only product. Accordingly, we deduced that cleroindicin A (**1**) was 7-hydroxy-1-oxospiro [3.5]-nonane.

Cleroindicin B (**2**) was obtained as a colorless oil. It was shown to have a molecular formula of $C_8H_{14}O_3$ from the EIMS (m/z 158 $[M]^+$, 140 $[M - H_2O]^+$, 122 $[M - 2H_2O]^+$, and 112 $[140 - C_2H_4]^+$). Its IR spectrum indicated the presence of hydroxyl and carbonyl groups. Compound **2** should have a ring and a carbonyl group according to the calculation of unsaturated degrees (n = 2). From the ^{13}C-NMR spectrum of **2**, only six carbon signals [δ 69.8 (s, C-1), 37.6 (2C, t, C-2, -6), 37.8 (2C, t, C-3, -5),211.5 (s, C-4), 44.4 (t, C-7), 58.8 (t, C −8)] were observed, indicating that compound **2** was also a symmetric molecule. The ^{1}H-NMR spectrum of **2** exhibited six groups of proton signals [δ 4.18 (2H, t, J = 6.6 Hz, H-8), 2.05 (2H, t, J = 6.6 Hz, H-7), 2.95 (2H, dt, J = 13.6, 6.2 Hz, H_{ax}-3,5), 2.32 (2H, dt, J = 13.6, 4.8 Hz, H_{eq}-3,5), 2.16 (2H, dt, J = 13.2, 4.8 Hz, H_{eq}-2,6), 1.84 (2H, dt, J = 13.2, 6.2 Hz, H_{ax}-2,6)]. Both H-7 and H-8 coupled with each other, splitting into two groups of triplets, suggesting that compound **2** contained a $-CH_2CH_2OH$ unit. Further consideration of its symmetry and NMR spectra readily established cleroindicin B as **2**.

Cleroindicin C (**3**): $[\alpha]_D$ −22.32° (c 0.37, MeOH), was also obtained as a colorless oil. Its HREIMS spectrum ([M] + 156.0761, calcd 156.0786) afforded the molecular formula of $C_8H_{12}O_3$. Analysis of the EIMS spectrum (m/z 156 $[M]^+$, 138 $[M - H_2O]^+$, and 128 $[M - CO]^+$) showed that compound **3** possessed hydroxyl and carbonyl groups that were confirmed by its IR spectrum. Such a compound should have two rings in addition to a carbonyl group on the basis of the calculation of its unsaturated degrees (n = 3). Compound **3** had one more ring than compound **2** but had same number of carbons and oxygens, suggesting a structural correlation between them. The NMR signals indicated that **3** was a cyclohexane−tetrahydrofuran derivative, and two configurational isomers were considered.

In structure **3**, two rings were connected with each other as indicated, while the alternative structure was inverted at C-9. In the ^{13}C-NMR spectrum of **3**, the only methine was assigned as C-9 (δ 84.6), which correlated with the H-9 [δ 4.25 (1H, t, J = 4.2 Hz)] from the ^{1}H-^{13}C COSY spectrum. The inverse structure at C-9 was easily excluded as H-9 did not exhibit a typical double doublet. Structure **3** was consistent with NMR information. The C-9 proton was equatorial; thus, it was possible to form two equal dihedral angles with the methylene protons at C-8. As a result, H-9 appeared as a triplet. The C-8 methylene protons also coupled with each other and exhibited two groups of characteristic double doublets [δ 2.97 (1H, dd, J = 15.7, 4.2 Hz), 2.76 (1H, dd, J = 15.7, 4.2 Hz)], owing to the chirality of C-9. The results also confirmed the carbonyl group at C-7. Similarly, the two C-3 protons showed two groups of multiple peaks (δ 2.07 m and 2.02 m) due to the chiral C-4. Therefore, cleroindicin C was identified as structure **3**. The CD spectrum showed a negative Cotton effect confirming the absolute configuration of **3** based on octant rules for ketones.[3,4]

Cleroindicin D (**4**), colorless oil, $[\alpha]_D$ + 1.55° (c 0.030, MeOH) gave an IR spectrum similar to that of **3**. Its molecular formula ($C_8H_{12}O_4$) was determined by EIMS (m/z 172 $[M]^+$, 154 $[M - H_2O]^+$ and 136 $[M - 2H_2O]^+$). The NMR spectra revealed that **4** had the same carbon skeleton as **3**. Compound **4** possessed one more hydroxy than **3** from its ^{13}C-NMR spectrum. One new oxymethine (δ 71.4) appeared and one methylene (δ 34.3) disappeared as compared to the spectrum of **3**. The additional hydroxy was confirmed at C-5, since the signals of C-4 and C-6 shifted downfield from δ 76.9 to 79.1 (+2.2 ppm) and from δ 35.8 to 42.7 (+6.9 ppm), respectively, while little variation at C-2, C-8, and C-9 was observed. Examining the ^{1}H-NMR spectrum of **4** led to the conclusion that 5-OH was in the α- orientation. On the basis of the ^{1}H-^{13}C COSY spectrum, the H-5 signal was determined as δ 4.36 (1H, t, J = 6.5 Hz), which coupled with H_{ax}-6 and H_{eq}-6 splitting into a triplet due to equal dihedral angles. Correspondingly, both H_{ax}-6 and H_{eq}-6 exhibited two groups of typical double doublets [δ 3.01 (1H, dd, J = 16.5, 6.5 Hz), 2.86 (1H, dd, J = 16.5, 6.5 Hz)], for they were in different environments owing to the existence of the chiral C-5. The signal of H-9 still remained a standard triplet [δ 4.34 (1H, t, J = 4.6 Hz)], and the signals of H_{ax}-8 and H_{eq}-8 were two groups of characteristic double doublets [δ 2.81 (1H, dd, J = 16.6, 4.6 Hz), 3.22 dd (1H, dd, J = 16.6, 4.6 Hz)]. All these observations indicated that the carbonyl group in compound **4** was also at C-7. Consequently, the structure of cleroindicin D was established as **4**.

Cleroindiin E (**5**), $[\alpha]_D$ +1.15° (*c* 0.011, MeOH), was obtained as colorless oil. Its IR spectrum only showed hydroxyl absorptions. The HREIMS spectrum ($[M]^+$ 158.0886, calcd 158.0943) of **5** afforded its molecular formula ($C_8H_{14}O_3$). The EIMS spectrum gave the molecular ion peak at *m/z* 158 $[M]^+$ and fragment ion peaks at *m/z* 140 $[M - H_2O]^+$ and 122 $[M - 2H_2O]^+$. Compound **5** had two rings from the calculation of unsaturated degrees ($n = 2$). In the ^{13}C-NMR spectrum of **5**, one methine (δ 66.0) bearing one hydroxy was apparent, and there was no signal indicating a carbonyl group. Thus, clerindicin E (**5**) was shown to be dihydrocleroindicin C (**3**). The ^{1}H-NMR spectrum showed that the 7-OH was equatorial since H-7 coupled with H_{ax}-6 and H_{ax}-8 splitting into a triplet (diaxial coupling, $J_1 = 10.8$ Hz) and then coupled with H_{eq}-6 and H_{eq}-8 (axial−equatorial coupling, $J_2 = 4.2$ Hz) into a triple triplet [δ 4.34 (1H, tt, $J = 10.8$, 4.2 Hz)]. Moreover, the triplet [δ 4.24 (1H t, $J = 4.0$ Hz)] belonging to H-9 was still observed, while both H_{ax}-8 and H_{eq}-8 appeared as multiplets at δ 2.48 and 2.28, respectively. Accordingly, cleroindcin E was identified as **5**.

Cleroindicin F (**6**), $[\alpha]_D$ −2.74° (*c* 0.016, MeOH), colorless oil, was shown to be an α,β-unsaturated ketone from its IR and UV spectra. Its molecular formula ($C_8H_{10}O_3$) was concluded from the EIMS spectrum (*m/z* 154 [M]$^+$, 136 $[M - H_2O]^+$, 110 $[M - C_2H_4O]^+$, 82 $[M - CO]^+$). In the ^{13}C-NMR spectrum of **6**, two olefinic methines [δ 150.2 (d, C-5), 128.1 (d, C-6)], a conjugated carbonyl group [δ 197.2 (s, C-7)], three methylenes [δ 66.5 (t, C-2), 40.6 (t, C-8), 40.4 (t, C-3)], one methine [δ 82.1 (d, C-9)] bearing oxygen, and one downfield quarternary carbon [δ 75.0 (s, C-4)] were exhibited. Its ^{1}H-NMR spectrum showed a pair of *Z*-double bond signals [δ 6.94 (1H, d, $J = 10.2$ Hz, H-5), 6.14 (1H, d, $J = 10.2$ Hz, H-6)], a typical H9 signal [δ 4.49 (1H, dd, $J = 4.8$, 4.0 Hz)], and an ABX system [δ 2.98 (1H, dd, $J = 16.5$, 4.8 Hz), 2.85 (1H, dd, $J = 16.5$, 4.0 Hz)] corresponding to C8 methylene signals. Since an α,β-unsaturated ketone was present, the dihedral angle between H-9 and H_{eq}-8 was no longer equal to that between H-9 and H_{ax}-8. Consequently, cleroindicin F (**6**) was deduced as a dehydrated derivative of cleroindicin D (**4**).

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO-20C-type polarimeter, and the CD spectrum was obtained on a J-500C-type spectrometer. IR spectra were recorded with a Perkin-Elmer 577 spectrometer. UV spectra were taken on a UV 210 spectrometer. NMR spectra were obtained using a Bruker AM-400 spectrometer with pyridine-d_5 and CD_3OD as solvents. NOESY: SW 2000Hz, D 1 s, 2 048 512 increments, 90° shifted sine-bell-squared apodization, zero-filled to 1024 in one dimension during processing, mixing time 1 s. MS were recorded on VG Auto Spec3000 spectrometer.

Plant Material. Plant material was collected in Xishuangbanna of Yunnan province and identified as *C. indicum* (L.) Kuntze. A voucher specimen is kept in the Herbarium of Kunming Institute of Botany, Yunnan, People's Republic of China.

Extraction and Isolation. Dried and powdered aerial parts (6 kg) of *C. indicum* were extracted with 95% EtOH (4 20L) under reflux to give a crude extract (320 g). The extract was dissolved in 50% EtOH and then defatted with petroleum ether (60−90 °C). After the removal of EtOH, the residue was extracted with EtOAc (5 × 2 L). The EtOAc extract (78 g) was chromatographed on a Si gel column eluting with $CHCl_3$−Me_2CO (5:1) to separate it into eight fractions (I−VIII).

Fraction II was subjected to column chromatography on Kiesel gel 60 (0.040−0.063 mm) eluting with $CHCl_3$−iPrOH (20:1) to afford cleroindicin A (**1**, 172 mg) and cleroindicin B (**2**, 68 mg). Part III was chromatographed on a medium-pressure column eluting with $CHCl_3$-MeOH (25:1) to yield cleroindicin C (**3**, 210 mg) and cleroindicin E (**5**, 140 mg). After repeated Si gel column chromatography eluting with $CHCl_3$-MeOH (25:1), cleroindicin D (**4**, 64 mg), cleroindicin F (**6**, 48 mg) were isolated from fractions V and VI.

Cleroindicin A (1): $C_8H_{14}O_2$, white needles, mp 56−57 °C; IR (KBr) ν_{max} 3300 (br), 2920, 2880, 1435, 1365, 1300, 1240, 1110, 1050, 1020, 965, 840 cm^{-1}; ^{1}H-NMR (C_5D_5N, 400 MHz) δ 4.21 (2H, t, $J = 6.6$ Hz, H-2), 3.92 (1H, tt, $J = 11.2$, 4.1 Hz, H-7), 2.30 (2H, m, H_{ax}-6 and H_{ax}-8), 2.08 (2H, m, H_{eq}-5 and H_{eq}-9), 2.04 (2H, m, H_{eq}-6 and H_{eq}-8), 2.02 (2H, t, $J = 6.6$ Hz, H-3), 1.54 (2H, dt, $J = 12.8$, 3.6, H_{ax}-5 and H_{ax}-9); ^{13}C-NMR (C_5D_5N, 100 MHz) δ 70.3 (s, C-4), 70.1 (d, C-7), 59.1 (t, C-2), 45.4 (t, C-3), 36.4 (t, C-5 and C-9), 31.9 (t, C-6 and C-8); HREIMS (70 eV) *m/z* 142.0945 $[M]^+$ (calcd 142.0994 for $C_8H_{14}O_3$); EIMS (70 eV) *m/z* $[M]^+$ 142 (18), $[M - C_2H_4 + H]^+$ 115 (42), $[115 - H_2O]^+$ 97 (71).

A. Acetylation of 1 Using Ac_2O/Pyridine (H_2O). Compound **1** (40 mg) was dissolved in pyridine (H_2O) (5 mL), and then Ac_2O (2 mL) was added. After 24 h at room temperature, the reaction residue was separated into **7** and **8**.

B. Acetylation of 1 Using Distilled Pyridine. Compound **1** (30mg) was dissolved in distilled pyridine (5 mL), and then Ac_2O (2 mL) was added into the reaction system. The subsequent procedures were same as in A. The reaction residue only provided **7** (35 mg).

Compound 7: $C_{12}H_{18}O_4$, colorless oil; ^{1}H-NMR (C_5D_5N, 400 MHz) δ 4.89 (1H, tt, $J = 10.5$, 3.8 Hz, H-7), 4.48 (2H, t, $J = 7.3$ Hz, H-2), 2.10 (2H, m, H_{ax}-6 and H_{ax}-8), 2.00 (6H, s, 2-Ac and 7-Ac), 1.93 (2H, m, H_{eq}-5 and H_{eq}-9), 1.91 (2H, t, $J = 7.3$ Hz, H-3), 1.88 (2H, m, H_{eq}-6 and H_{eq}-8), 1.46 (2H, dt, $J = 12.8$, 4.2 Hz, H_{ax}-5 and H_{ax}-9); ^{13}C-NMR (C_5D_5N, 100 MHz) δ 170.9 (s, 2-Ac*C*O), 170.3 (s, 7-Ac*C*O), 72.9 (d, C-7), 68.5 (s, C-4), 61.4 (t, C-2), 41.8 (t, C-3), 35.7 (t, C-5 and C-9), 27.5 (t, C-6 and C-8), 21.3 (2-AcMe), 21.0 (7-AcMe); EIMS (70 eV) *m/z* $[M + H]^+$ 227 (25), $[M - Ac + H]^+$ 184 (55), $[184 - C_2H_4 + H]^+$ 157 (64), $[184 - Ac + H]^+$ 142 (51), $[142 - H_2O]^+$ 124 (97).

Compound 8: $C_{12}H_{18}O_4$, colorless oil; ^{1}H-NMR (C_5D_5N, 400 MHz) δ 5.11 (1H, brs, H-7), 4.55 (2H, t, $J = 7.3$ Hz, H-2), 2.10 (2H, m, H_{ax}-6 and H_{ax}-8), 2.00 (6H, s, 2-Ac and 7-Ac), 1.98 (2H, m, H_{eq}-5 and H_{eq}-9), 1.91 (2H, t, $J = 7.3$ Hz, H-3), 1.88 (2H, m, H_{eq}-6 and H_{eq}-8), 1.72 (2H, dt, $J = 13.2$, 4.4 Hz, H_{ax}-5 and H_{ax}-9); ^{13}C-NMR (C_5D_5N, 100 MHz) δ 170.9 (s, 2-Ac*C*O), 170.3 (s, 7-Ac*C*O), 70.6 (d, C-7), 69.1 (s, C-4), 61.3 (t, C-2), 41.2 (t, C-3), 33.7 (t, C-5 and C-9), 26.7 (t, C-6 and C-8), 21.3 (2-AcMe), 21.0 (7-AcMe); its EIMS spectrum was near identical to that of **7**.

Cleroindicin B (2): $C_8H_{14}O_3$, colorless oil; IR (dry film) ν_{max} 3300, 2930, 1700 (br), 1420, 1250, 1050, 840

cm^{-1}; ^{1}H-NMR (C_5D_5N, 400 MHz) δ 4.18 (2H, t, J = 6.6 Hz, H-8), 2.95 (2H, dt, J = 13.6, 6.2 Hz, H_{ax}-3 and H_{ax}-5), 2.32 (2H, dt, J = 13.6, 4.8 Hz, H_{eq}-3 and H_{eq}-5), 2.16 (2H, dt, J = 13.2, 4.8 Hz, H_{eq}-2 and H_{eq}-6), 2.05 (2H, t, J = 6.6 Hz, H-7), 1.84 (2H, dt, J = 13.2, 6.2 Hz, H_{ax}-2 and H_{ax}-6); ^{13}C-NMR (C_5D_5N, 100 MHz) δ 211.5 (s, C-4), 69.8 (s, C-1), 58.8 (t, C-8), 44.4 (t, C-7), 37.8 (t, C-3 and C-5), 37.6 (t, C-2 and C-6); EIMS (70 eV) *m/z* $[M]^+$ 158 (55), $[M - H_2O]^+$ 140 (52), $[M - 2H_2O]^+$ 122, $[140 - C_2H_4]^+$ 112 (60).

Cleroindicin C (3): $C_8H_{12}O_3$, $[\alpha]_D$ −22.32° (*c* 0.082, MeOH), colorless oil; IR (dry film) ν_{max} 3300 (br), 2940, 2860, 1705, 1400, 1250, 1060, 845 cm^{-1}; ^{1}H-NMR (C_5D_5N, 400 MHz) δ 4.25 (1H, t, J = 4.2 Hz), 3.91 (2H, m, H-2), 2.97 (1H, dd, J = 15.7, 4.2 Hz, H_{ax}-8), 2.76 (1H, dd, J = 15.7, 4.2 Hz, H_{eq}-8), 2.32 (1H, ddd, J = 15.8, 10.8, 3.6 Hz, H_{ax}-6), 2.22 (1H, m, H_{ax}-5), 2.13 (1H, m, H_{eq}-5), 2.07 (1H, m, H-3a), 2.02 (1H, m, H-3b), 1.63 (1H, ddd, J = 11.6, 6.2, 3.4 Hz, H_{eq}-6); ^{13}C-NMR (C_5D_5N, 100 MHz) δ 209.9 (s, C-7), 84.6 (d, C-9), 76.9 (s, C-4), 66.3 (t, C-2), 43.1 (t, C-8), 40.9 (t, C-3), 35.8 (t, C-6), 34.3 (t, C-5); HREIMS (70 eV) *m/z* $[M]^+$ 156.0761 (calcd 156.0786); EIMS (70 eV) *m/z* $[M]^+$ 156 (41), $[M - H_2O]^+$ 138 (16), $[M - CO]^+$ 128 (42).

Cleroindicin D (4): $C_8H_{12}O_3$, $[\alpha]_D$ + 1.55° (*c* 0.095, MeOH), colorless oil; IR (dry film) ν_{max} 3300 (br), 2920, 1700 (br), 1420, 1250, 1050, 845 cm^{-1}; ^{1}H-NMR (C_5D_5N, 400 MHz) δ 4.36 (1H, t, J = 6.5 Hz, H-5), 4.34 (1H, t, J = 4.6 Hz, H-9), 3.97 (2H, m, H-2), 3.22 (1H, dd, J = 16.6, 4.6 Hz, H_{eq}-8), 3.01 (1H, dd, J = 16.5, 6.5 Hz, H_{ax}-6), 2.86 (1H, dd, J = 16.5, 6.5 Hz, H_{eq}-6), 2.81 (1H, dd, J = 16.6, 4.6 Hz, H_{ax}-8), 2.69 (2H, m, H-3); ^{13}C-NMR (C_5D_5N, 100 MHz) δ 208.4 (s, C-7), 83.9 (d, C-9), 79.1 (s, C-4) , 71.4 (d, C-5), 66.6 (t, C-2), 43.8 (t, C-8), 42.7 (t, C-6), 39.2 (t, C-3); EIMS (70 eV) *m/z* $[M]^+$ 172 (48), $[M - H_2O]^+$ 154 (13), $[M - 2H_2O]^+$ 140 (12), $[140 - CO]^+$ 112 (73).

Clerindicin E (5): $C_8H_{14}O_3$, $[\alpha]_D$ +1.15° (*c* 0.046, MeOH), colorless oil; IR (dry film) ν_{max} 3300 (br), 2950 (br), 1430 (br), 1270, 1170, 920, 850 cm^{-1}; ^{1}H-NMR (C_5D_5N, 400 MHz) δ 4.34 (1H, tt, J = 10.7, 4.2 Hz, H-7), 4.24 (1H, t, J = 4.0 Hz, H-9), 4.05 (1H, m, H-2a), 3.94 (1H, m, H-2b), 2.48 (1H, m, H_{eq}-8), 2.24 (1H, m, H_{ax}-8), 2.18 (1H, m, H_{eq}-6), 2.15 (2H, m, H-3), 2.12 (1H, m, H_{eq}-5), 2.03 (1H, m, H_{ax}-6), 1.93 (1H, m, H_{ax}-5); ^{13}C-NMR (C_5D_5N, 100 MHz) δ 82.3 (d, C-9), 75.3 (s, C-4), 66.0 (d, C-7), 65.4 (t, C-2), 39.8 (t, C-3), 36.8 (t, C-8), 33.2 (t, C-5), 31.8 (t, C-6); HREIMS (70 eV) *m/z* $[M]^+$ 158.0886 (calcd 158.0943 for $C_8H_{14}O_3$); EIMS (70 eV) *m/z* $[M]^+$ 158 (7), $[M - H_2O]^+$ 140 (71), $[M - 2H_2O]^+$ 122 (54).

Cleroindicin F (6): $C_8H_{10}O_3$, $[\alpha]_D$ −2.74° (*c* 0.016, MeOH), colorless oil; UV (EtOH) ν_{max} (log) 218.5 (4.68) nm; IR (dry film) ν_{max} 3370 (br), 2940, 2870, 1675, 1375, 1260, 840 cm^{-1}; ^{1}H-NMR (C_5D_5N, 400 MHz) δ 6.94 (1H, d, J = 10.2 Hz, H-5), 6.14 (1H, d, J = 10.2 Hz, H-6), 4.49 (1H, dd, J = 4.8, 4.0 Hz, H-9), 4.05 (1H, m, H-2a), 3.87 (1H, q, J = 8.2 Hz, H-2b), 2.98 (1H, dd, J = 16.5, 4.8 Hz, H_{ax}-8), 2.85 (1H, dd, J = 16.5, 4.0 Hz, H_{eq}-8), 2.44 (1H, m, H-3a), 2.20 (1H, m, H-3b); ^{13}C-NMR (C_5D_5N, 100 MHz) δ 197.2 (s, C-7), 150.2 (d, C-5), 128.1 (d, C-6), 82.1 (d, C-9), 75.0 (s, C-4), 66.5 (t, C-2), 40.6 (t, C-8), 40.4 (t, C-3); EIMS (70 eV) *m/z* $[M]^+$ 154 (5), $[M - H_2O]^+$ 136 (12), $[M - C_2H_4O]^+$ 110, $[110 - CO]^+$ 82.

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References and Notes

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