



## NEW XENIA DITERPENOIDS FROM A *XENIA* SPECIES OF A SOFT CORAL<sup>1</sup>

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**Abstract:** Seven new xenia diterpenoids including seco-type variants have been isolated from a soft coral, *Xenia* sp., and their structures elucidated on the basis of spectroscopy.  
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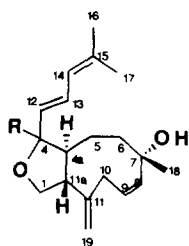
A number of xenicane-type diterpenoids, containing a cyclononane skeleton, have been isolated from soft corals, gorgonians, and algae.<sup>2</sup> In the course of our continuing investigation of *Xenia* species,<sup>3-7</sup> we have examined a specimen collected in the area of Sata Cape, Kagoshima prefecture. Acetone was used for extraction, instead of methanol, to avoid the formation of artifacts due to methanolysis.<sup>5</sup> The concentrated acetone extract was partitioned between dichloromethane and water. Bioassay guided fractionation of the dichloromethane extract, which showed antimicrobial activity against *Echerichia coli* and *Bacillus subtilis*, using a combination of silica gel, gel filtration on Sephadex LH-20, and finally reversed phase HPLC. This yielded six new xenia diterpenoids: xeniaethers F (1), G (2), and H (3), isoxeniatine C (4), azamials A (5) and B (6) as an inseparable mixture, and xenicinedial 7, together with five known compounds, xeniaethers A (8),<sup>3</sup> B (9),<sup>4</sup> and C (10),<sup>6</sup> and azamilides B (11)<sup>7</sup> and H (12).<sup>6</sup> In this report, we describe their isolation and structure characterization of 1-7.

### RESULTS AND DISCUSSION

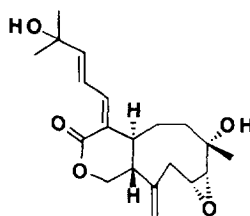
The major compound was xeniaether F (1), C<sub>38</sub>H<sub>64</sub>O<sub>4</sub>, which displayed a UV maximum at 240 nm suggesting a conjugated diene system and had IR absorption bands assigned to a hydroxyl group (3450 cm<sup>-1</sup>), an acyl group (1740 cm<sup>-1</sup>), and an olefinic group (1660 and 1630 cm<sup>-1</sup>). The <sup>1</sup>H NMR spectrum was similar to that of xeniaether A (8),<sup>3</sup> except for additional resonances due to a long chain aliphatic ester group (δ 0.88; 3H, t, *J*=6.8 Hz, CH<sub>3</sub>CH<sub>2</sub>-; δ 1.25, s, -(CH<sub>2</sub>)<sub>*n*</sub>-; δ 2.31; 2H, t, *J*=7.5 Hz, -CH<sub>2</sub>CH<sub>2</sub>COO-). The acyl group was located at C-3 by the downfield shift of H-3 (δ 4.10; 2H, s) compared to the same position in 8 (δ 3.56; 2H, AB, *J*=11.6 Hz). In the negative ion FABMS spectrum, a fragmentation peak, *m/z* 283, corresponding to

$C_{17}H_{35}COO^-$  indicated the presence of a stearoyl group. Therefore, xeniaether F (1) was assigned to be 3-*O*-stearylxeniaether A.

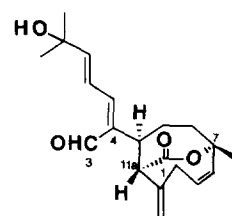
Xeniaethers G (2),  $C_{36}H_{60}O_4$ , and H (3),  $C_{39}H_{66}O_4$ , were eluted together with 1 and could not be distinguished from 1 by the  $^1H$  and  $^{13}C$  NMR data, suggesting that they contained different acyl groups. The presence of a palmitoyl group in 2 and a nonadecanoyl group in 3 was supported by the negative fragmentation ions,  $m/z$  255 corresponding to  $C_{15}H_{31}COO^-$  and  $m/z$  297 corresponding to  $C_{18}H_{37}COO^-$  in the negative ion FABMS spectrum, as observed in azamilides C and D.<sup>7</sup> The structures of xeniaethers G (2) and H (3) were thus determined to be 3-*O*-palmitylxeniaether A and 3-*O*-octadecanylexeniaether A.



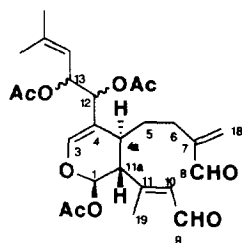
- 1 R= $\beta$ - $CH_2OCOC_{17}H_{35}$   
 2 R= $\beta$ - $CH_2OCOC_{15}H_{31}$   
 3 R= $\beta$ - $CH_2OCOC_{18}H_{37}$   
 8 R= $\beta$ - $CH_2OH$   
 9 R= $\alpha$ - $CH_2OH$   
 10 R= $\beta$ - $CH_2OH$ , 8(9)- $\alpha$ -epoxide



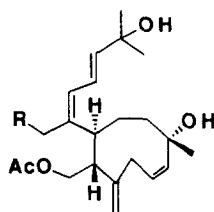
4  
13 8(9)*Z*



5  
6 4(12)*E*



7



11 R= $OCOC_{15}H_{31}$   
 12 R= $OCOC_{17}H_{35}$ , 8(9)- $\alpha$ -epoxide

Isoxeniatine C (4),  $C_{20}H_{28}O_5$ , displayed a UV maximum at 273 nm suggesting an  $\alpha,\beta,\gamma,\delta$ -unsaturated carbonyl and contained absorption bands corresponding to a hydroxyl group ( $3450\text{ cm}^{-1}$ ), an acyl group ( $1710\text{ cm}^{-1}$ ), and a conjugated diene ( $1630\text{ cm}^{-1}$ ) in the IR spectrum. The  $^1H$  NMR spectrum was similar to that of isoxeniatine A (13),<sup>4</sup> except for two new resonances ( $\delta$  2.80; 1H, d,  $J=4.4$  Hz, H-8,  $\delta$  3.10; 1H, dt,  $J=4.4$  and 10.3 Hz, H-9) that were ascribed to methine protons on an epoxide. *Trans* fusion of the two rings was indicated by the DIFNOE data (Figure 1.). H-1 $\alpha$  ( $\delta$  3.99; 1H, t,  $J=11.4$  Hz) showed an NOE correlation with H-4a ( $\delta$  3.54, 1H, m, 3.4%), whereas H-1 $\beta$  ( $\delta$  4.10; 1H, dd,  $J=4.8$  and 11.4 Hz) showed a correlation with

H-11a ( $\delta$  2.61; 1H, dt,  $J=4.8$  and 11.4 Hz, 3.9%). The major conformer of the 9-membered ring was elucidated by the observation of NOEs between H-4a and H-10 $\alpha$  ( $\delta$  ca 2.74; 1H, m, 8.9%), between H-11a and H-19 ( $\delta$  5.22; 1H, br s, 3.9%), between H-9 and H-19 ( $\delta$  5.24; 1H, br s, 2.0%) and H-8 (7.3%), and between H-8 and H-18 ( $\delta$  1.41; 3H, s, 2.3%). Thus, the stereochemistry of the epoxide and that of the C-18 methyl group was assigned to be  $\alpha$  and  $\beta$ , respectively. Isoxeniatine C (4) was, therefore, 8(9)- $\alpha$ -epoxyisoxeniaine A.

Azamials A (5) and B (6) were isolated as inseparable stereoisomers and showed IR absorptions indicative of a hydroxyl group (3410  $\text{cm}^{-1}$ ), an aldehyde (2770 and 1660  $\text{cm}^{-1}$ ), a lactone carbonyl (1710  $\text{cm}^{-1}$ ), and a conjugated diene (1630  $\text{cm}^{-1}$ ). In the UV spectrum, the presence of an  $\alpha,\beta,\gamma,\delta$ -unsaturated carbonyl was suggested by a UV maximum at 281 nm. Eight degrees of unsaturation was indicated by the molecular formula  $\text{C}_{20}\text{H}_{28}\text{O}_5$ . Resonances due to eight olefins [ $\delta$  117.3 (t), 118.9 (d), 125.7 (d), 131.5 (d), 139.1 (s), 141.0 (s), 146.5 (d), and 151.3 (d)], a lactone carbonyl [ $\delta$  173.3 (s)], and an aldehyde [ $\delta$  188.8 (d)] in the  $^{13}\text{C}$  NMR spectrum of the major compound 5 accounted for seven double-bond equivalents, suggesting that 5 is a bicyclic diterpenoid. The diterpenoid seemed to be a xenia diterpenoid on the basis of the following data: Resonances due to three methyl groups ( $\delta$  1.40, 3H x 3, s, Me-16, Me-17, and Me-18) on carbons bearing oxygen and three olefinic protons of the conjugated diene system corresponding to H-12 ( $\delta$  6.73, 1H, d,  $J=11.9$  Hz), H-13 ( $\delta$  7.26; 1H, dd,  $J=11.9$  and 14.7 Hz), and H-14 ( $\delta$  6.21, 1H, d,  $J=14.7$  Hz) were observed. The presence of another isolated double bond was indicated by resonances corresponding to H-8 ( $\delta$  5.24; 1H, dd,  $J=2.6$  and 12.0 Hz) and H-9 ( $\delta$  5.89, 1H, ddd,  $J=5.1$ , 10.3, and 12.0 Hz), and the latter proton was coupled to H-10 ( $\delta$  2.69; 1H, dd,  $J=10.1$  and 14.5 Hz,  $\delta$  3.10; 1H, m). The two broad singlets at  $\delta$  4.38 and 4.98 were due to the exomethylene group H-19, as already observed in 1-4. The characteristic UV for the conjugated carbonyl system and the characteristic lowfield chemical shift of the  $\beta$  proton (H-13) suggested that the aldehyde or the lactone carbonyl group was attached at C-4. The presence of the aldehyde at C-4 was confirmed by the observation of an NOE from H-11a to the aldehydic proton (22.7%) as depicted in Figure 2. The position of the lactone carbonyl was determined to be at C-1 from the lowfield chemical shift of C-11a ( $\delta_{\text{C}}$  55.4) compared to those of 1-4. The lactone group was, therefore, formed with a carboxyl group at C-11a and a hydroxyl group at C-7, because the hydroxyl group at C-15 is located too far from the C-1 to esterize. The stereochemistry of the lactone group was tentatively proposed to be in the configuration shown (Figure 2) by the NOE experiments and by the fact that the hydroxyl group at C-7 and the substituent at C-11a in other xenia diterpenoids so far isolated have been in the *cis* position.<sup>3,4,6,7</sup> Thus, NOEs between H-8 and H-18 (1.7%) and H-9 (15.7%), between H-10 $\alpha$  ( $\delta$  2.69) and H-9 (3.2%) and H-19 ( $\delta$  4.98, 5.7%), between H-10 $\beta$  ( $\delta$  3.10; 1H, m) and H-10 $\alpha$  and H-5 $\alpha$  ( $\delta$  ca 2.6; 1H, overlapped) (H-10 $\alpha$  + H-5 $\alpha$ , 21.9%), and between H-11a and H-4a (5.9%) and H-19 ( $\delta$  4.38, 4.4%) were found. Furthermore, the broad singlet due to H-4a suggesting that the dihedral angle between C-4a and C-11a is approximately 90° is also consistent with the structure of 5. Azamial B (6) is the geometric isomer of azamial A (5). The 4(12)-diene moiety was determined to be *E* by the lowfield chemical shift of H-12 ( $\delta$  6.94; 1H, d,  $J=11.7$  Hz) and an NOE between H-3 ( $\delta$  9.42; 1H, s) and H-12

(19.3%). Despite repeated HPLC chromatography, it was not possible to obtain **5** completely free of **6**, and it is possible that **5** and **6** are photoisomers. Azamilal A and B were the second example of xenia diterpenoids from the genus *Xenia* with an opened A-ring.<sup>7</sup>

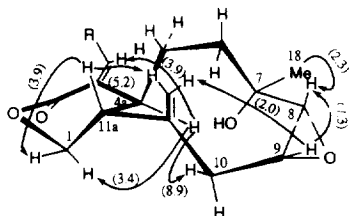


Figure 1. NOEs (%) observed for **4**.  
R=side chain.

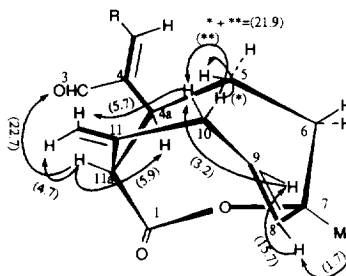


Figure 2. NOEs (%) observed for **5**.  
R=side chain.

Xenicindial **7** showed absorption bands due to a conjugated aldehyde group ( $1850$  and  $1670\text{ cm}^{-1}$ ) and an ester carbonyl ( $1740$  and  $1225\text{ cm}^{-1}$ ) in the IR spectrum. The molecular formula  $\text{C}_{26}\text{H}_{34}\text{O}_9$  indicated ten degrees of unsaturation, and nine of these were accounted for by the NMR data which showed the presence of four olefinic bonds [ $\delta_{\text{C}}$   $111.7$  (s),  $119.0$  (d),  $128.4$  (d),  $134.4$  (t),  $140.6$  (s),  $142.3$  (s),  $149.5$  (s), and  $158.8$  (s)], three acetyl groups [ $\delta_{\text{H}}$   $2.01$  (3H x 2, s) and  $2.10$  (3H, s);  $\delta_{\text{C}}$   $20.9$  (q),  $21.0$  (q), and  $21.2$  (q);  $169.2$  (s),  $\delta$   $170.0$  (s), and  $170.1$  (s)], and two aldehyde groups [ $\delta_{\text{H}}$   $9.56$  (1H, s) and  $10.0$  (1H, d,  $J=7.5$  Hz);  $\delta_{\text{C}}$   $191.0$  (d) and  $194.2$  (d)]. Therefore, compound **7** was concluded to be monocyclic. The  $^1\text{H}$ - $^1\text{H}$  COSY spectrum resolved the side chain from C-12 to C-17 and an acetylated cyclic acetal system similar to the one present in xenicin.<sup>8</sup> The two olefinic methyl groups Me-16 and Me-17 were weakly coupled to an olefinic proton H-14 ( $\delta$   $5.13$ ; 1H, br d,  $J=9.3$  Hz), which in turn was coupled to H-13 ( $\delta$   $5.70$ ; 1H, dd,  $J=5.7$  and  $9.3$  Hz) which is attached to a carbon carrying an acetyl group. H-13 was further coupled to H-12 ( $\delta$   $5.28$ ; 1H, d,  $J=5.7$  Hz) which is also attached to a carbon bearing an acetyl group. The presence of the pyran ring indicated that the cyclononane ring common to most compounds from this coral species had been cleaved. One of the two aldehydic protons ( $\delta$   $10.0$ ; 1H, d,  $J=7.5$  Hz) was coupled to an olefinic proton ( $\delta$   $5.96$ ; 1H, br d,  $J=7.5$  Hz), which in turn was weakly coupled to olefinic methyl protons ( $\delta$   $2.23$ ; 3H, br s), indicating a 3-substituted 2-butenal moiety. The presence of a 2-substituted 2-propenal moiety was evident from two broad lowfield singlets ( $\delta$   $6.07$  and  $6.33$ ; 1H each) due to the exomethylene protons, which were conjugated with the second aldehyde group ( $\delta$   $9.56$ ). The remaining two methylene carbons were assigned to C-5 ( $\delta$   $24.9$ , t) and C-6 ( $\delta$   $30.3$ , t) in the  $^{13}\text{C}$  NMR spectrum. Information on the connectivity of the 3-substituted 2-butenal moiety and C-11a resulted from NOEs between the olefinic proton at  $\delta$   $5.96$  and H-1 (4.6%) and H-11a (2.7%). The 2-substituted-2-propenal moiety was therefore attached to C-6. Thus, the gross structure of **7** was completed. The geometry of the double bond at C-10 was determined to be *E* by the chemical shift of the C-19 methyl carbon ( $\delta_{\text{C}}$   $17.1$ ) and an NOE (4.1%) between H-19 and H-9. The *trans* relationship between H-4a and H-11a

was determined from the value of the coupling constant ( $J=3.3$  Hz) between H-4a and H-11a, coinciding with the fact that all xenia diterpenoids isolated to date had a *trans* ring junction.<sup>2</sup> The long-range coupling between H-1 and H-4a was observed in the <sup>1</sup>H-<sup>1</sup>H COSY spectrum, implying that the protons occurred on the same face of the ring system. The large coupling constant ( $J=9.3$  Hz) between H-12 and H-13 suggested that H-12 and H-13 were *anti*, and hence C-12 and C-13 had R\* and S\* configurations, or S\* and R\* configurations, respectively. This is only the third example of a xenia diterpene containing a cleaved cyclononane ring.<sup>9,10</sup> Although two xenia diterpenoids possessing an aldehyde group have so far been isolated only from the seaweeds of the genus *Dctiyota*,<sup>11,12</sup> this is the first isolation of such a diterpenoid from marine animals.

Many variants of xenia diterpenoids might be expected to be found in *Xenia* sp., because no investigation of their chemical constituents has been as extensive as that for the cembranoid group of the metabolites isolated from soft corals.<sup>2</sup> We have isolated diterpenoids containing a tetrahydrofuran like **1**, **2**, and **3** from only two kinds of *Xenia* species, collected in Kagoshima prefecture.<sup>3,4,6</sup> Furthermore, most of them contained acyl fatty chains of C<sub>16</sub>, C<sub>18</sub>, and C<sub>19</sub>. The nonadecanoic acid is less common. Xenia diterpenoids with an opened A-ring like **5** and **6** and an opened B-ring like **7** are also rarely found. In general, compounds possessing an aldehyde group, especially an  $\alpha,\beta$ -unsaturated aldehyde group, are likely to demonstrate biological activity. However, the activity test could not be performed because of their insufficient amount. Antibacterial activity tests were done on compounds **1-4** and **8-12** using the paper disc method (8 mm diam. and 1.5 mm thick). Xeniaethers A (**8**) and C (**10**) displayed antibacterial activity against *Echerichia coli* at 250  $\mu\text{g/disk}$  and 100  $\mu\text{g/disk}$ , respectively.

## EXPERIMENTAL

**Extract and isolation.** Specimens of *Xenia* sp. were collected at depths of -1 m at Sata Cape, Kagoshima prefecture. The reference sample (collection #153) was identified by Dr. Y. Imahara (Wakayama Prefectural Museum of Natural History). The organisms (wet weight: 4.1 Kg) were extracted with acetone immediately after collection. The acetone extract was suspended in H<sub>2</sub>O and extracted with CH<sub>2</sub>Cl<sub>2</sub>. The CH<sub>2</sub>Cl<sub>2</sub> was dried over Na<sub>2</sub>SO<sub>4</sub>, filtered, and evaporated to dryness. A portion of (30 g) of the CH<sub>2</sub>Cl<sub>2</sub> extract (76 g) which showed antibacterial activity against *E. coli* and *B. subtilis* was absorbed on silica gel and subjected to column chromatography of silica gel packed in hexane, being collected as follows: A: CH<sub>2</sub>Cl<sub>2</sub>-hexane, 1:1, B: CH<sub>2</sub>Cl<sub>2</sub>-hexane, 1:4, C: CH<sub>2</sub>Cl<sub>2</sub>-hexane, 1:4 and CH<sub>2</sub>Cl<sub>2</sub>, D: acetone-CH<sub>2</sub>Cl<sub>2</sub>, 1:19, E: acetone-CH<sub>2</sub>Cl<sub>2</sub>, 1:19 and 1:9, F: acetone-CH<sub>2</sub>Cl<sub>2</sub>, 1:9 and 1:1, G: acetone, and H: EtOH. Fr E was chromatographed on silica gel using CH<sub>2</sub>Cl<sub>2</sub>-acetone, increasing the proportion of acetone to elute the column. The fractions eluted with CH<sub>2</sub>Cl<sub>2</sub> and then acetone-CH<sub>2</sub>Cl<sub>2</sub> (1:49) were applied to a column of Sephadex LH-20 and eluted with acetone-CHCl<sub>3</sub> (1:1) to yield a residue. The residue was purified by silica gel chromatography with AcOEt-hexane (1:9) and (3:7) and then reversed-phase C<sub>18</sub> chromatography with the range from CH<sub>3</sub>CN-H<sub>2</sub>O (87:13) to (1:1), yielding **1** (12.1 mg), **2** (2.8 mg), **3** (0.8 mg), and **7** (1.0 mg). Fr. F was subjected to silica gel chromatography with EtOH-CH<sub>2</sub>Cl<sub>2</sub> (1:49) to give residue (a). Further elution with EtOH-CH<sub>2</sub>Cl<sub>2</sub> (1:19) resulted in residue (b). A mixture of **5** and **6** and **10**, **11**, and **12** was finally

isolated from residue (a) by reversed-phase C<sub>18</sub> chromatography with CH<sub>3</sub>CN-H<sub>2</sub>O increasing the portion of H<sub>2</sub>O. Elution with CH<sub>3</sub>CN-H<sub>2</sub>O (19:1) gave **11** (4.4 mg) and **12** (2.2 mg), and elution with CH<sub>3</sub>CN-H<sub>2</sub>O (3:7) yielded compound **10** (6.3 mg). Compounds **4** (2.5 mg), **8** (30.1 mg), and **9** (1.9 mg) were separated from the residue (b) by pre. TLC with AcOEt-hexane (3:2) and then by reversed-phase HPLC with CH<sub>3</sub>CN-H<sub>2</sub>O (9:11 and 2:3) or 2-PrOH-H<sub>2</sub>O (3:17).

Analytical TLC was carried out on aluminium sheets (Kieselgel 60 F<sub>254</sub>, Merck) using Me<sub>2</sub>CO-CH<sub>2</sub>Cl<sub>2</sub> (1:19; system S1), MeOH-EtOEt (3:97; system S2), or EtOAc-hexane (1:1; system S3). R<sub>f</sub> values were for **1**: 0.55, **2**: 0.55, **3**: 0.55, and **4**: 0.18 (S1), for **5**: 0.33 (S2), for **7**: 0.42, **8**: 0.18, and **9**: 0.31 (S1), and for **10**: 0.42, **11**: 0.38, and **12**: 0.47 (S3).

All known compounds **8-12** were identified by comparing the spectroscopic data with those of the authentic samples.

The IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR data of Xeniaethers F (**1**), G (**2**), and H (**3**) could not be distinguished from one another.

**Xeniaether F-H (1-3).** IR (film) 3450, 1740, 1660, and 1630 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 0.88 (3H, d, *J*=6.8 Hz, CH<sub>3</sub>CH<sub>2</sub>-), 1.25 [s, -(CH<sub>2</sub>)<sub>n</sub>-], 1.33 (3H, s, Me-18), *ca* 1.49 (1H, m, H-5β), 1.76 and 1.77 (3H each, s, Me-16 and Me-17), *ca* 1.85 (2H, H-5α and H-6α), 2.02-2.08 (1H, m, H-6β), 2.31 (2H, t, *J*=7.5 Hz, -CH<sub>2</sub>CH<sub>2</sub>COO-), 2.78 (1H, dt, *J*=4.6 and 9.0 Hz, H-4a), 2.86-2.94 (2H, m, H-10α and H-11a), 3.34 (1H, dd, *J*=7.0 and 11.8 Hz, H-10β), 3.77 (1H, t, *J*=8.6 Hz, H-1α), 3.98 (1H, t, *J*=8.6 Hz, H-1β), 4.10 (2H, s, H-3), 4.91 and 4.94 (1H each, br s, H-19), 5.45-5.54 (3H, m, H-8, H-9, and H-12), 5.81 (1H, br d, *J*=10.6 Hz, H-14), and 6.49 (1H, dd, *J*=10.6 and 15.4 Hz, H-13); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 14.1 [CH<sub>3</sub>(CH<sub>2</sub>)<sub>n</sub>-], 18.4 (C-17), 22.7-34.5 [CH<sub>3</sub>(CH<sub>2</sub>)<sub>n</sub>COO-], 23.7 (C-5), 26.0 (C-16), 33.0 (C-18), 35.0 (C-10), 39.2 (C-6), 50.0 (C-11a), 50.6 (C-4a), 66.1 (C-3), 70.5 (C-1), 74.0 (C-7), 85.6 (C-3), 112.7 (C-19), 124.6 (C-12), 126.3 (C-13), 129.3 (C-9), 131.3 (C-14), 136.0 (C-11), 136.8 (C-8), 146.5 (C-15), and 173.7 (CH<sub>3</sub>COO-).

**Xeniaether F (1).** Oil, [α]<sub>D</sub> +45.7° (*c* 0.13, MeOH); UV λ<sub>max</sub> 240 nm (ε 13700); FABMS: *m/z* 623 [M+K]<sup>+</sup> and 283 [C<sub>17</sub>H<sub>35</sub>COO]<sup>-</sup>.

**Xeniaether G (2).** Oil, [α]<sub>D</sub> +41.5° (*c* 0.13, MeOH); FABMS: *m/z* 579 [M+Na]<sup>+</sup> and 255 [C<sub>15</sub>H<sub>31</sub>COO]<sup>-</sup>.

**Xeniaether H (3).** Oil, [α]<sub>D</sub> +80.0° (*c* 0.05, MeOH); UV λ<sub>max</sub> 240 nm (ε 19600); FABMS: *m/z* 621 [M+Na]<sup>+</sup> and 297 [C<sub>18</sub>H<sub>37</sub>COO]<sup>-</sup>.

**Isoxeniatine C (4).** Oil, [α]<sub>D</sub> -28.0° (*c* 0.05, MeOH); UV λ<sub>max</sub> 273 nm (ε 12800); IR (film) 3450, 1710, and 1630 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.39 (3H x 2, s, Me-16 and Me-17), 1.41 (3H, s, Me-18), 1.73-1.80 (3H, m, H-5 and H-6β), *ca* 2.01 (1H, m, H-6α), 2.61 (1H, dt, *J*=4.8 and 12.4 Hz, H-11a), *ca* 2.74 (2H, m, H-10), 2.80 (1H, d, *J*=4.4 Hz, H-8), 3.10 (1H, dt, *J*=4.4 and 10.3 Hz, H-9), 3.54 (1H, m, H-4a), 3.99 (1H, t, *J*=11.4, H-1α), 4.10 (dd, *J*=4.8 and 11.4 Hz, H-1β), 5.22 and 5.24 (1H each, br s, H-19), 6.17 (1H, d, *J*=15.6 Hz, H-14), 6.63 (1H, dd, *J*=1.8 and 11.0 Hz, H-12), and 7.74 (1H, dd, *J*=11.0 and 15.6 Hz, H-13); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 28.9 (C-5 or C-6), 29.4 and 29.5 (C-16 and C-17), 29.7 (C-6 or C-5), 32.3 (C-18),

34.8 (C-10), 37.6 (C-4a), 48.2 (C-11a), 60.2 (C-9), 61.7 (C-8), 71.0 (C-15 or C-7), 71.5 (C-1), 72.0 (C-7 or C-15), 120.0 (C-19), 124.1 (C-13), 129.0 (C-4), 140.5 (C-12), 142.1 (C-11), 149.9 (C-14), and 165.3 (C-3); HREIMS:  $m/z$  330.1850 [ $M^+$ -H<sub>2</sub>O], calcd for C<sub>20</sub>H<sub>26</sub>O<sub>4</sub>,  $m/z$  330.1830].

**Azamials A (5) and B(6).** Oil, UV  $\lambda_{\max}$  281 nm ( $\epsilon$  11300); IR (film) 3410, 2770, 1710, 1660, and 1630 cm<sup>-1</sup>; HREIMS:  $m/z$  330.1844 ( $M^+$ ), calcd for C<sub>20</sub>H<sub>26</sub>O<sub>4</sub>,  $m/z$  330.1830.

**Azamial A (5):** <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.40 (3H x 3, s, Me-16, Me-17, and Me-18), H-5 $\alpha$  ( $\delta$  ca 2.6; 1H, overlapped), 2.69 (1H, dd,  $J$ =10.1 and 14.5 Hz, H-10 $\alpha$ ), 3.10 (1H, m, H-10 $\beta$ ), 3.19 (1H, m, H-4a), 3.99 (1H, br s, H-11a), 4.38 and 4.98 (1H each, br s, H-19), 5.24 (1H, dd,  $J$ =2.6 and 12.0 Hz, H-2.6 and H-12.0, H-8), 5.89 (1H, ddd,  $J$ =5.1, 10.3, and 12.0 Hz, H-9), 6.21 (1H, d,  $J$ =14.7 Hz, H-14), 6.73 (1H, d,  $J$ =11.9 Hz, H-12), 7.26 (1H, dd,  $J$ =11.9 and 14.7 Hz, H-13), and 10.3 (1H, s, H-3); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  25.6 (C-5), 29.8 (C-16 and C-17), 31.4 (C-18), 35.3 (C-10 or C-6), 38.0 (C-4a), 40.2 (C-6 or C-10), 55.4 (C-11a), 71.2 (C-15), 85.4 (C-7), 117.3 (C-19), 118.9 (C-13), 125.7 (C-9), 131.5 (C-8), 139.1 (C-4 or C-11), 141.0 (C-11 or C-4), 146.5 (C-12), 151.3 (C-14), 173.3 (C-1), and 188.8 (C-3).

**Azamial B (6):** <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.40 (3H x 3, s, Me-16, Me-17, and Me-18), 2.73 (1H, dd,  $J$ =10.1 and 13.7 Hz, H-10 $\alpha$ ), ca 3.10 (1H, obscured, H-10 $\beta$ ), 3.25 (1H, m, H-4a), 3.97 (1H, br s, H-11a), 4.55 and 4.93 (1H each, br s, H-19), 5.30 (1H, dd,  $J$ =2.6 and 12.1 Hz, H-8), 5.95 (1H, ddd,  $J$ =5.5, 10.3, and 12.1 Hz, H-9), 6.35 (1H, d,  $J$ =15.0, H-14), 6.78 (1H, dd,  $J$ =11.7 and 15.0 Hz, H-13), 6.94 (1H, d,  $J$ =11.7 Hz, H-12), and 9.42 (1H, s, H-3); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  25.9 (C-5), 29.5 and 29.7 (C-16 and C-17), 31.2 (C-18), 35.0 (C-10 or C-6), 39.5 (C-4a), 41.0 (C-6 or C-10), 55.4 (C-11a), 71.1 (C-15), 85.9 (C-7), 117.3 (C-19), 118.9 (C-13), 125.7 (C-9), 131.5 (C-8), 132.7 (C-4 or C-11), 134.8 (C-11 or C-4), 146.5 (C-12), 151.3 (C-14), and 188.8 (C-3).

**Xeniaciindial (7).** Oil, [ $\alpha$ ]<sub>D</sub> +15.0° ( $c$  0.03, MeOH); UV  $\lambda_{\max}$  243 nm ( $\epsilon$  13100); IR (film) 1850, 1740, 1670, and 1225 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>)  $\delta$  1.74 (3H x 2, s, Me-16 and Me-17), 2.01 (3H x 2, s, Ac x 2), 2.10 (3H, s, Ac), 2.23 (3H, br s, Me-19), ca 2.40 (1H, m, H-4a), 2.75 (1H, t,  $J$ =3.3 Hz, H-11a), 5.13 (1H, br d,  $J$ =9.3 Hz, H-14), 5.28 (1H, d,  $J$ =5.7 Hz, H-12), 5.70 (1H, dd,  $J$ =5.7 and 9.3 Hz, H-13), 5.96 (1H, br d,  $J$ =7.5 Hz, H-10), 6.07 (1H, br s, H-18), 6.17 (1H, d,  $J$ =3.3 Hz, H-1), 6.33 (1H, br s, H-18), 6.51 (1H, br s, H-3), 9.56 (1H, s, H-8), and 10.0 (1H, d,  $J$ =7.5 Hz, H-9); <sup>13</sup>C NMR (CDCl<sub>3</sub>)  $\delta$  17.1 (C-19), 18.7 (C-17), 20.9, 21.0, and 21.2 (Ac x 3), 24.9 (C-5), 25.9 (C-16), 30.3 (C-6), 34.7 (C-4a), 46.2 (C-11a), 70.3 (C-13), 74.1 (C-12), 90.4 (C-1), 111.7 (C-4), 119.0 (C-14), 128.4 (C-10), 134.4 (C-18), 140.6 (C-15), 142.3 (C-3), 149.5 (C-7), 158.8 (C-11), 169.2, 170.0, and 170.1 (Ac x 3), 191.0 (C-9), and 194.2 (C-8); EIMS:  $m/z$  430 ( $M^+$ -AcOH), 363 [ $M^+$ -Me<sub>2</sub>CH=CH(OAc)], and 303 [ $M^+$ -Me<sub>2</sub>CH=CH(OAc)-AcOH, base peak].

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