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Umbellactal, a novel diterpenoid from the Formosan soft coral *Xenia umbellata*

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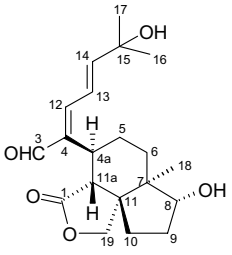
Abstract—Umbellactal, isolated from the soft coral *Xenia umbellata,* is an unprecedented diterpenoid. The structure of umbellactal was established by extensive analysis of spectroscopic data.

The soft corals of genus *Xenia* are rich in diterpenoids.[1] As part of our search for novel bioactive substances from marine and terrestrial organisms,[2–5] the soft coral *Xenia umbellata* Lamarck was studied because CH_2Cl_2 extracts showed significant cytotoxicity to A549 (human lung adenocarcinoma), HT-29 (human colon adenocarcinoma), and P-388 (mouse lymphocytic leukemia) cell cultures as determined by standard procedures.[6] Bioassay-guided fractionation resulted in the isolation of a novel cytotoxic diterpenoid (novel skeleton), umbellactal (**1**).



1

Compound **1** was isolated as a colorless oil, $[\alpha]_D^{25}$ −30 (*c* 0.1, $CHCl_3$). The IR spectrum of **1** exhibited absorptions due to hydroxyl (3480 cm^{-1}), γ-lactone (1760 cm^{-1}) and conjugated aldehyde (1715 cm^{-1}) groups. The presence of the conjugated aldehyde was also confirmed by the UV spectrum [λ_{max} 235 nm]. HRESIMS suggested a molecular formula of $C_{20}H_{28}O_5$ ($[M+H]^+$ *m/z* 349.2009 (Δ +1 mmu)).

The structure of **1** was completely solved by a combination of 1D and 2D NMR methods. The carbon resonances at δ_C 194.9 (CH), 139.9 (qC), 151.7 (CH), 120.3 (CH), and 153.4 (CH), in the ^{13}C NMR and DEPT spectra showed the presence of an α,β,γ,δ-unsaturated aldehyde (Table 1). The carbonyl carbon signal at δ_C 177.4 along with the lactonic methylene carbon (γ) signal at δ_C 74.3, methine carbon (α) signal at δ_C 51.4, and a quarternary carbon (β) signal at δ_C 49.3 indicated the presence of an γ-lactone. Furthermore, the presence of the other two sp^3 oxygenated carbons was inferred from the carbon signals at δ_C 71.2 (qC) and 73.6 (CH). Four methylene groups were deduced from the DEPT signals at δ_C 23.1, 30.0, 28.9, and 35.0, two methine signals at δ_C 46.3 and 51.4, two quarternary carbon signals at δ_C 43.0 and 49.3, and, finally, three methyl signals at δ_C 16.0, 29.4, 29.8.

The ^1H NMR spectrum confirmed the presence of an α,β,γ,δ-unsaturated aldehyde by the fact that signals were observed at δ_H 9.40, 6.92, 6.60, and 6.38. In addition, an oxygenated methylene [δ_H 4.07 (d, $J = 9.0$ Hz), 4.44 (d, $J = 9.0$ Hz)] and an oxygenated methine [δ_H 4.48 (t, $J = 9.0$ Hz)] were observed. Two intense singlet signals are also observed at δ_H 1.37 (s, 3H), 1.39 (s, 3H), and this correspond to two methyl groups. In this manner the seven degrees of unsaturation present in **1** were established.

Keywords: Xenibellal; *Xenia umbellata*.
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Table 1. ^{1}H and ^{13}C NMR data of **1** (500 and 100 MHz, respectively, in $CDCl_3$) (δ, in ppm relative to TMS)

Pos.	δ_H[a]	δ_C[a]
1		177.4 (qC)
3	9.40 s	194.9 (CH)
4		139.9 (qC)
4a	2.66 t (12.0)[b]	46.3 (CH)
5	2.27 m, 1.38 m	23.1 (CH_2)
6	1.76 m	30.0 (CH_2)
7		43.0 (qC)
8	4.48 t (9.0)	73.6 (CH)
9	1.72 m, 2.37 m	28.9 (CH_2)
10	1.72 m, 1.96 m	35.0 (CH_2)
11		49.3 (qC)
11a	2.83 d (12.0)	51.4 (CH)
12	6.92 d (11.0)	151.7 (CH)
13	6.60 dd (15.0, 11.0)	120.3 (CH)
14	6.38 d (15.0)	153.4 (CH)
15		71.2 (qC)
16	1.37 s	29.4 (CH_3)
17	1.39 s	29.8 (CH_3)
18	0.86 s	16.0 (CH_3)
19	4.07 d (9.0), 4.44 d (9.0)	74.3 (CH_2)

[a] Assigned by DEPT, COSY, NOESY, HSQC, and HMBC experiments.
[b] Coupling constant in hertz in parentheses.

The combined use of ^{1}H–^{1}H COSY and HMQC on **1** allowed us to distinguish three spin systems (see **a**–**c** in Fig. 1) and two methyl groups linked to an oxygenated quaternary carbon. An HMBC experiment was used to assemble the skeletal fragments through quaternary carbons and heteroatoms. Thus, these substructures were connected through HMBC correlations between the protons H-12 (δ_H 6.92) and the carbons C-4 (δ_C 139.9), between the protons H_2-19 (δ_H 4.07 and 4.44) and the carbons C-10 (δ_C 35.0), C-7 (δ_C 43.0), C-11 (δ_C 49.3), C-11a (δ_C 51.4), and C-1 (δ_C 177.4), between the methyl protons Me-18 (δ_H 0.86) and carbons C-6 (δ_C 30.0), C-7, C-11, and C-8 (δ_C 73.6), and between H-4a and C-1. These relationships are represented in Figure 1.

All these data allowed us to identify compound **1** as a new diterpenoid with a novel skeleton. With the gross structure of **1** in hand, the relative stereochemistry of compound **1** was deduced from NOESY correlations (Fig. 2), and by comparison of its spectroscopic data to those of *Xenia* diterpenes.[2,7–9] The *E* geometry was

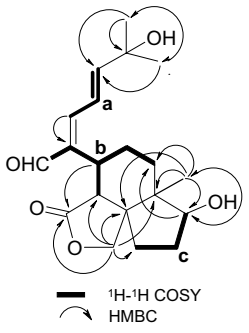

Figure 1. Key COSY and HMBC correlations of **1**.

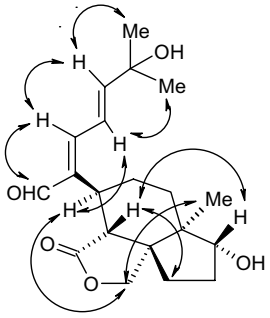

Figure 2. Key NOESY correlations of **1**.

assigned to the $\Delta^{4,12}$ double bond on the basis of the observation of a NOESY correlation between H-3 and H-12, and between H-13 and H-4a. The *E* geometry of the Δ^{13} double bond was established by the large coupling constant observed between H-13 and H-14 ($J = 15.0$ Hz). The large coupling constant ($J = 12.0$ Hz) between H-4a and H-11a suggested that they have a configuration opposite of each other.[2,7–9] The NOE correlations from H_2-19 to Me-18/H-4a and NOE correlations from H-11a to H-8/H_2-10 were observed. This suggests that H-4a, H_2-19, and Me-18 are on the α face of the molecule while H-11a, H_2-10, and H-8 are on the opposite, β face, of the molecule.

Umbellactal (**1**) exhibited cytotoxicity against P-388 cell line with ED_{50} of 3.6 μg/mL. Boigenetically, **1** may be a double cyclization ([2+2+2] reaction) product of the delactonized analogue of azamial B.[7]

Acknowledgements

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References and notes

1. Blunt, J. W.; Copp, B. R.; Munro, M. H. G.; Northcote, P. T.; Prinsep, M. R. *Nat. Prod. Rep.* **2004**, *21*, 1–49, and previous papers in this series.
2. El-Gamal, A. H.; Wang, S.-K.; Duh, C.-Y. *Org. Lett.* **2005**, *7*, 2023–2025.
3. El-Gamal, A. H.; Wang, S.-K.; Duh, C.-Y. *Tetrahedron. Lett.* **2005**, *46*, 4499–4500.
4. Duh, C.-Y.; El-Gamal, A. H.; Wang, S.-K. *Tetrahedron Lett.* **2003**, *44*, 9321–9322.
5. Duh, C.-Y.; Wang, S.-K.; Chia, M.-C.; Chiang, M. Y. *Tetrahedron Lett.* **1999**, *40*, 6033–6035.
6. Hou, R.-S.; Duh, C.-Y.; Chiang, M. Y.; Lin, C.-N. *J. Nat. Prod.* **1995**, *58*, 1126–1130.
7. Iwagawa, T.; Masuda, T.; Okamura, H.; Nakatani, M. *Tetrahedron* **1996**, *52*, 13121–13128.
8. Duh, C.-Y.; El- Gammal, A. A. H.; Chiang, C.-Y.; Chu, C.-J.; Wang, S.-K.; Dai, C.-F. *J. Nat. Prod.* **2002**, *65*, 1882–1885.
9. Iwagawa, T.; Amano, Y.; Hase, T.; Shiro, M. *Tetrahedron* **1995**, *51*, 11111–11118.