



## Untenolide A, a new polyketide from an Okinawan marine sponge *Plakortis* sp.

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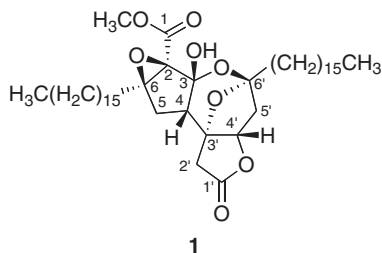
Untenolide A

### ABSTRACT

A new polyketide, untenolide A (**1**), has been isolated from an Okinawan marine sponge *Plakortis* species, and the structure was elucidated from spectroscopic data and X-ray analysis. Untenolide A (**1**) is a new polyketide possessing a fused-pentacyclic skeleton with two hexadecanyl chains.

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Marine sponges of the genus *Plakortis* are known to be a rich source of unique peroxy aliphatic acids and esters.<sup>1</sup> During our search for new metabolites from Okinawan marine sponges, we have isolated some polyketides with unique skeletons from the genus *Plakortis*.<sup>2–9</sup> Recently, we investigated the extracts of an Okinawan marine sponge *Plakortis* sp. (SS-614) and isolated untenolide A (**1**), a new polyketide possessing a fused-pentacyclic skeleton with two hexadecanyl chains. In this Letter, we describe the isolation and structure elucidation of **1**.



The sponge *Plakortis* sp. (SS-614, 0.60 kg, wet wt) collected off Unten Port, Okinawa, was extracted with MeOH. EtOAc-soluble materials of the extract were separated by a C<sub>18</sub> column (MeOH/H<sub>2</sub>O → MeOH/CHCl<sub>3</sub>) and silica gel columns (*n*-hexane/EtOAc and *n*-hexane/CHCl<sub>3</sub>) to give untenolide A (**1**, 10.3 mg, 0.0017%, wet

wt),<sup>10</sup> together with manzamenones A,<sup>2,11,12</sup> B,<sup>2</sup> and K,<sup>6</sup> and plakervulin A.<sup>7,13</sup>

Untenolide A (**1**) was obtained as an optically inactive colorless solid. The ESIMS spectrum of **1** showed the pseudomolecular ion peak at *m/z* 769 (M+Na)<sup>+</sup>, and the molecular formula of **1** was revealed to be C<sub>45</sub>H<sub>78</sub>O<sub>8</sub> by HRESIMS data [*m/z* 769.56147 (M+Na)<sup>+</sup>, Δ +2.03 mmu]. IR absorptions indicated the existence of hydroxy (3385 cm<sup>-1</sup>) and ester carbonyl (1783, and 1747 cm<sup>-1</sup>) functionalities. The <sup>1</sup>H and <sup>13</sup>C NMR data (Table 1), and analysis of the HMQC spectra of **1** implied the presence of two ester carbonyl carbons (δ<sub>C</sub> 174.4 and δ<sub>C</sub> 167.4 in CDCl<sub>3</sub>) and long aliphatic chains. Two quaternary carbons were assigned as (hemi)acetal carbons from their chemical shifts (δ<sub>C</sub> 101.3 and δ<sub>C</sub> 108.7 in CDCl<sub>3</sub>, respectively). The presence of an oxymethine (δ<sub>C</sub> 84.4 and δ<sub>H</sub> 5.12 in CDCl<sub>3</sub>) connected to ester carbonyl and three quaternary carbons bearing an oxygen atom (δ<sub>C</sub> 85.7, δ<sub>C</sub> 72.0, and δ<sub>C</sub> 66.8) was also deduced.

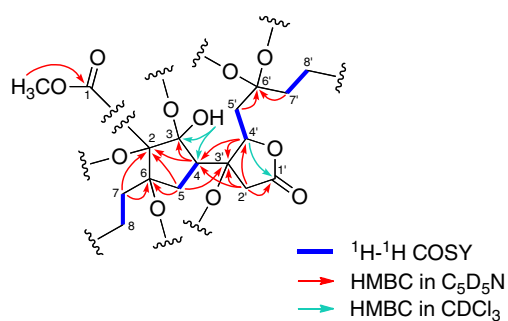
Inspection of the <sup>1</sup>H–<sup>1</sup>H COSY spectrum of **1** disclosed connectivities of C-4 to C-5, C-7 to C-8, C-4' to C-5', and C-7' to C-8'. The presence of a cyclopentane ring (C-2 to C-6) was revealed from HMBC correlations for H-4/C-2, H-4/C-3, H-5/C-2, and H-5/C-6. HMBC correlations for 3-OH/C-3 and 3-OH/C-4 suggested that C-3 was a hemiacetal carbon and a hydroxy group was attached to C-3. HMBC cross-peaks of H-7/C-2 and H-7/C-6 indicated that an alkyl chain was attached to C-6. The presence of a γ-lactone ring (C-1' to C-4' and 4'-O) was indicated from HMBC correlations for H-2'/C-1', H-2'/C-3', H-2'/C-4', and H-4'/C-3'. Connection of those two rings was suggested from HMBC cross-peaks of H-5/C-3', H-2'/C-4, and H-4'/C-4. Connectivity of C-5' and C-7' through an acetal carbon at C-6' was deduced from HMBC cross-peaks of H-5'/C-6' and H-7'/C-6'. The HMBC correlations between methoxy protons

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**Table 1**  
<sup>1</sup>H and <sup>13</sup>C NMR data of untenolide A (**1**)

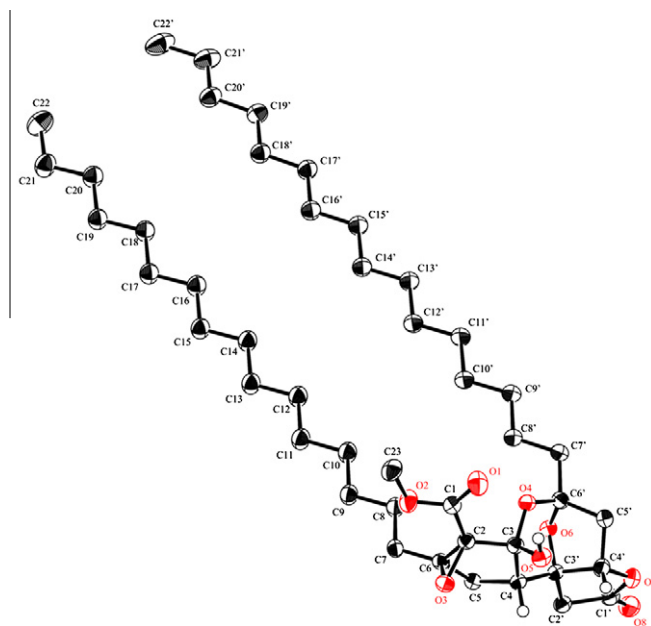
Position	$\delta_{\text{H}}^{\text{a}}$	$\delta_{\text{C}}^{\text{b}}$	Position	$\delta_{\text{H}}^{\text{c}}$	$\delta_{\text{C}}^{\text{d}}$
1		167.4	1		166.9
2		66.8	2		69.9
3		101.3	3		102.9
3-OH	3.97 (1H, br s)				
4	1.99 (1H, dd, 9.6, 7.8)	40.1	4	2.50 (1H, dd, 9.6, 7.8)	42.4
5a	2.13 (1H, dd, 13.7, 9.6)	29.0	5a	2.38 (1H, dd, 13.7, 9.6)	29.5
5b	2.05 (1H, dd, 13.7, 7.8)		5b	2.20 (1H, dd, 13.7, 7.8)	
6		72.0	6		71.4
7	1.92 (2H, m)	29.3	7	1.91 (2H, m)	30.4
8–21	1.1–1.6 (28H, br s)	29.0–31.8 (14C)	8	1.55 (2H, m)	25.8
			9–21	1.1–1.4 (26H, br s)	29.6–32.1 (13C)
22	0.86 (3H, t, 6.8)	14.0	22	0.86 (3H, t, 6.8)	14.3
1'		174.4	1'		174.8
2'a	2.65 (1H, d, 17.8)		2a'	3.03 (1H, d, 18.0)	38.5
2'b	2.48 (1H, d, 17.8)		2'b	2.98 (1H, d, 18.0)	
3'		85.7	3'		87.0
4'	5.12 (1H, dd, 6.6, 2.0)	84.4	4'	5.52 (1H, dd, 6.6, 1.9)	85.1
5'a	2.92 (1H, dd, 14.3, 6.7)	43.2	5'a	3.19 (1H, dd, 14.3, 6.5)	43.9
5'b	2.06 (1H, dd, 14.3, 2.0)		5'b	2.17 (1H, dd, 14.3, 2.0)	
6'		108.7	6'		108.6
7'	1.72 (2H, m)	37.2	7'	1.94 (2H, m)	38.2
8'–21'	1.1–1.6 (28H, br s)	29.0–31.8 (14C)	8'	1.72 (2H, m)	23.9
			9'–21'	1.1–1.4 (26H, br s)	29.6–32.1 (13C)
22'	0.86 (3H, t, 6.8)	14.0	22'	0.86 (3H, t, 6.8)	14.3
–OCH <sub>3</sub>	3.80 (3H, s)	52.4	–OCH <sub>3</sub>	3.52 (3H, s)	51.7

<sup>a</sup> 400 MHz in CDCl<sub>3</sub>.<sup>b</sup> 150 MHz in CDCl<sub>3</sub>.<sup>c</sup> 600 MHz in C<sub>5</sub>D<sub>5</sub>N.<sup>d</sup> 150 MHz in C<sub>5</sub>D<sub>5</sub>N.**Figure 1.** Selected 2D NMR correlations for untenolide A (**1**).

( $\delta_{\text{H}}$  3.80 in CDCl<sub>3</sub>) and ester carbonyl carbon ( $\delta_{\text{C}}$  167.4 in CDCl<sub>3</sub>) indicated the presence of a methyl ester (Fig. 1). Since four out of seven unsaturations were accounted for, **1** was inferred to possess three more rings. However, the gross structure of **1** was not elucidated from 2D NMR data.

Untenolide A (**1**) was crystallized from benzene as monoclinic crystal (P21/c, (#14), mp 94–98 °C).<sup>14</sup> The single crystal X-ray diffraction analysis revealed the gross structure and relative stereochemistry of **1**. The crystal consisted of a pair of enantiomers, suggesting that **1** was a racemate. The ORTEP drawing of one enantiomer of **1** and crystal lattice structure of **1** were shown in Figures 2 and 3, respectively.

A possible biogenetic path for untenolide A (**1**) is proposed as shown in Scheme 1. 3,6-Dioxo-4-docosenoic acid (**W**) has been proposed to be a hypothetical common key intermediate for the metabolites of *Plakortis* sponges.<sup>8</sup> Untenolide A (**1**) seems to be generated from two molecules of **W**. The bicyclo compound (**X**) could be derived from **W** as a racemic mixture, while the cyclopentadienone (**Y**) might be generated from another **W** through unte-

**Figure 2.** ORTEP drawing of untenolide A (**1**).

none A.<sup>4,6</sup> Subsequently, **Y** binds to the convex side of **X** to afford a compound (**Z**), from which untenolide A (**1**) could be generated by the formation of hemiacetal and the epoxidation of cyclopentene-one unit.

Untenolide A (**1**) is a new polyketide possessing a fused-pentacyclic skeleton with two hexadecanyl chains. Untenolide A (**1**) did not show cytotoxicities against P388 and L1210 murine leukemia, and KB human epidermoid carcinoma cells (IC<sub>50</sub> >10.0 μg/mL) in vitro.

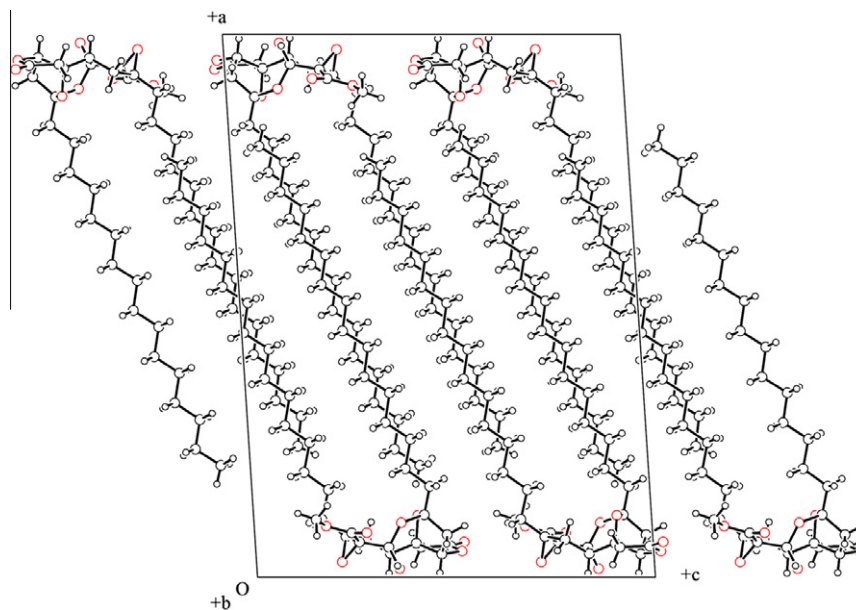
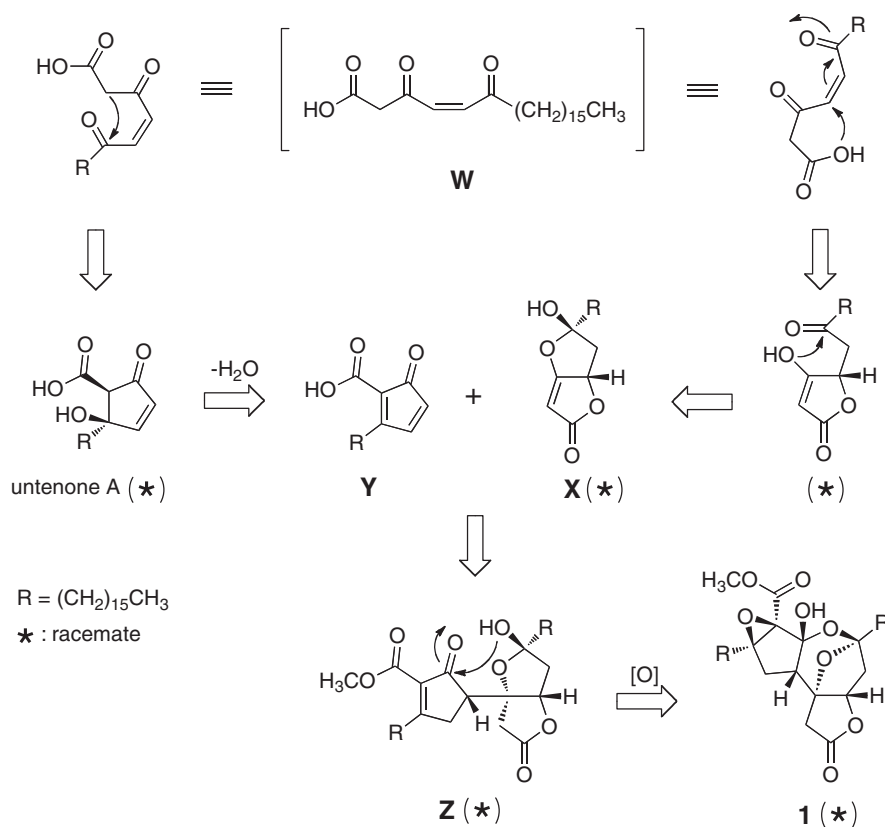


Figure 3. Crystal lattice structure of untenolide A (1).



Scheme 1. Possible biogenetic path for untenolide A (1).

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10. Untenolide A (**1**): colorless monoclinic crystal (benzene); mp 94–98 °C;  $[\alpha]_D^{21} \simeq 0$  (c 1.0, CHCl<sub>3</sub>); IR (KBr)  $\nu_{\max}$  3385 (br), 2919, 2850, 1783, and 1747 cm<sup>-1</sup>; <sup>1</sup>H and <sup>13</sup>C NMR, see Table 1; ESIMS (pos.) *m/z* 769 [(M+Na)<sup>+</sup>]; HRESIMS (pos.) *m/z* 769.56147 [(M+Na)<sup>+</sup>, calcd for C<sub>45</sub>H<sub>78</sub>O<sub>8</sub>Na, 769.55944].
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14. The X-ray crystal structure has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number CCDC 778959.