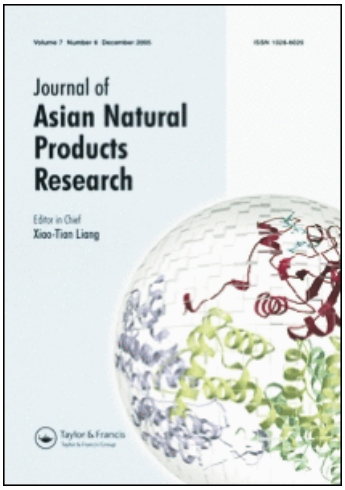

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ATEMOYACIN E, A *BIS*-TETRAHYDROFURAN ANNONACEOUS ACETOGENIN FROM *ANNONA ATEMOYA* SEEDS

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Atemoyacin E (**1**), a new adjacent *bis*-tetrahydrofuran annonaceous acetogenin was isolated and characterized from the seeds of *Annona atemoya*.

Keywords: Annonaceous acetogenins; *Annona atemoya* seeds; Atemoyacin E

INTRODUCTION

Annona atemoya Hort (Annonaceae) is a fruit tree native to Australia. In our previous study on this plant, four new *bis*-THF acetogenins, atemoyacin A, B, C, D, and about fifteen known acetogenins have been isolated from its roots and seeds [1]. We report, herein, the isolation of another new *bis*-THF acetogenin from the seeds of *Annona atemoya*, named atemoyacin E (**1**), as well as a known compound, octadecanoic acid. The planar structure of **1** and the relative stereochemistry of the bis-THF ring unit in **1** was elucidated by spectroscopic methods (Fig. 1).

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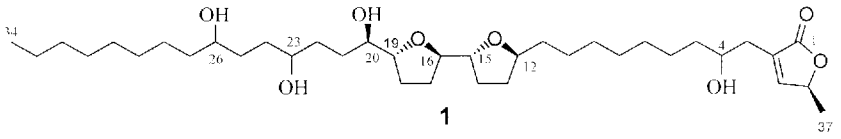

1

FIGURE 1 The structure of **1** and the relative configuration of its THF segment.

RESULTS AND DISCUSSION

Compound **1** was isolated as a yellow wax, m.p. 51–52°C, $[\alpha]_D = +21.8$ (c 0.22, MeOH). The molecular formula of **1** was established to be $C_{37}H_{66}O_8$ by HRFABMS which gave ion peak at *m/z* 661.4636 for the $[M+Na]^+$ (calcd. 661.4650), indicating its molecular weight of 638.

The spectral data of **1** showed an IR carbonyl absorption at 1748 cm^{-1}, a UV (MeOH) band at λ_{max} 208 nm ($\log \varepsilon = 4.04$), proton signals at δ 7.19 (H-35), 5.06 (H-36), 2.52 (H-3a), 2.40 (H-3b), 1.43 (H-37) in the ^1H NMR, and carbon resonances at δ 174.53 (C-1), 151.73 (C-35), 131.20 (C-2), 77.93 (C-36), 69.94 (C-4), 33.34 (C-3), 19.09 (C-37) in the ^{13}C NMR (Tab. I). These are all characteristic spectral features for the γ-methylated α,β – unsaturated γ-lactone ring with a 4-OH moiety, which was also supported by the positive Kedde reaction and the fragment ions at *m/z* 141 and 123 (cleavage between C-4 and C-5) in EIMS (Fig. 2).

The existence of four free hydroxyl groups in **1** was indicated by a prominent IR OH absorption at 3427 cm^{-1}, and four peaks at δ 74.40, 74.20, 71.64, 69.94 in ^{13}C NMR. The presence of an adjacent *bis*-THF ring system in **1** was suggested by the proton signals at δ 3.84 (H-12, H-15, H-16, H-19) in ^1H NMR and the carbon signals at δ 83.21 (C-19), 82.67 (C-16), 82.21 (C-15), 79.33 (C-12) in the ^{13}C NMR. As indicated by the carbon signal at δ 79.33 (C-12) in ^{13}C NMR [2] and the ^1H-^1H COSY experiment, there was only one hydroxyl flanking the THF rings, as in the gigantecin [3], bullatalicin [4].

The carbon skeleton and the location of the *bis*-THF ring unit was established by the analysis of EIMS of **1** and its TMS derivative (**1a**) (Fig. 2). The fragmentation pattern observed showed the *bis*-THF ring unit was located between C-12 and C-20. The relative stereochemistry between C-19 and C-20 of **1** was indicated as *threo* by comparing the ^1H NMR signals for H-20 (δ 3.41) and ^{13}C NMR resonacnces of **1** for C-19 (δ 83.2) and C-20 (δ 74.4) with those of compounds of known relative sterochemistry [5]. The proton peaks at δ 3.84 (H-15, H-16) in ^1H NMR of **1** suggested the relative

TABLE I NMR Data of **1** (^{1}H/600 MHz, ^{13}C/150 MHz, in $CDCl_3$)

Position	δ_H	δ_C
1	–	174.53
2	–	131.20
3a	2.52 dd	33.34
3b	2.40 dt	–
4	3.84 m	69.94
5	1.48 m	37.28
6 ~ 10	1.26 brs	25.48 ~ 31.84
11	1.63 m	35.60
12	3.84 m	79.33
13a	1.47 m	29.61
13b	2.02 m	–
14a	1.47 m	29.41
14b	1.63 m	–
15	3.84 m	82.21
16	3.84 m	82.67
17a	1.63 m	29.41
17b	1.94 m	–
18a	1.63 m	29.31
18b	1.94 m	–
19	3.84 m	83.24
20	3.41 m	74.40
21	1.63 m	31.88
22	1.63 m	32.26
23	3.41 m	71.64
24	1.63 m	32.58
25	1.63 m	33.34
26	3.60 m	74.20
27	1.63 m	35.60
28 ~ 32	1.26 brs	25.48 ~ 31.88
33	1.29 m	22.65
34	0.88 t	14.06
35	7.19 m	151.73
36	5.06 dd	77.93
37	1.43 d	19.09

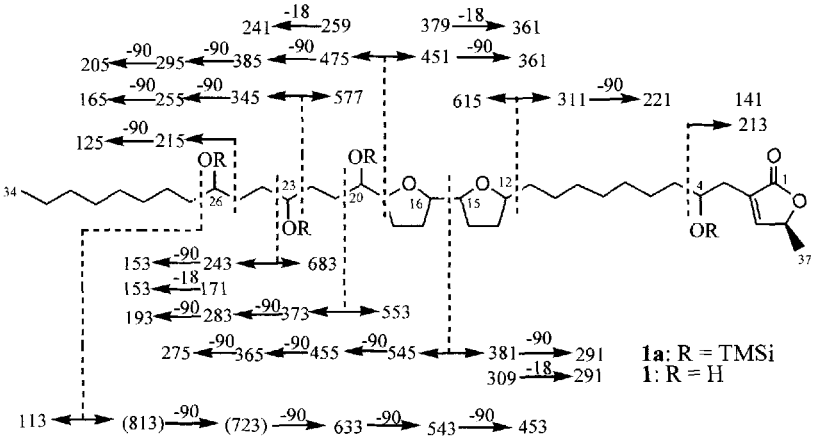

FIGURE 2 EIMS fragmentation of **1** and its TMS derivative **1a**.

stereochemistry between C-15 and C-16 was also *threo* [2]. The ^{1}H and ^{13}C NMR data for the methines and methylenes in the rings suggested the relative configurations of the two THF rings (C12/C15 and C16/C19) were both *trans* [2, 6]. Therefore the relative stereochemistry of the adjacent *bis*-THF ring with one flanking hydroxyl between C-12 and C-20 was *trans/threo/trans/threo*.

Comparison of the ^{1}H and ^{13}C NMR data of **1** with those of bulladecin [7], rollidecin A and rollidecin B [8] indicated that the structure of **1** was very similar to those of the mentioned three acetogenins. All of them have an adjacent *bis*-THF ring with one flanking hydroxyl, and a C-4 carbinol center. The remaining two hydroxyl groups of bulladecin, rollidecin A and rollindecin B were vicinal and located at the terminal alkyl chains respectively, which were proved by δ 3.60, 3.60 for the two methine protons and δ 74.5, 74.7 for the two oxygen bearing carbon in bulladecin, δ 3.54, 3.60 and δ 74.8, 75.4 in Rollidecin A and δ 3.39 – 3.42, 3.39 – 3.42 and δ 74.9, 75.6 in rollindecin B respectively. While ^{1}H and ^{13}C NMR data of **1** showed the ^{1}H values at δ 3.41, 3.60 for the two methine protons, and ^{13}C values at δ 71.64, 74.2 for the two secondary hydroxylated carbons, which suggested that these two hydroxyl groups in **1** were not vicinal. Furthermore EIMS fragmentations of **1** and **1a** showed the two hydroxyl groups were located at C-23 and C-26 respectively (Fig. 2).

In conclusion, compound **1** was a new annonaceous acetogenin, which has an adjacent *bis*-THF unit with one flanking hydroxyl. The relative stereochemical relationship of the THF system was *trans/threo/trans/threo* as illustrated in Figure 2.

Compound **2** was determined as octadecanoic acid by comparing the ^{1}H NMR and MS data of **2** with those of octadecanoic acid [9]. In addition, the mixed m.p. of **2** and octadecanoic acid didn't depressed, and they had the same R_f of TLC and retention time of HPLC.

EXPERIMENTAL SECTION

General Experiment Procedures

Melting points were determined on a Yanagimoto-MP-S2 apparatus and are uncorrected. Optical rotation was measured on a Perkin-Elmer 241 MC polarimeter. UV spectra was taken on a HP 8451A Diode Array spectrophotometer. IR data was recorded on a FTS-185 spectrometer. ESIMS and EIMS data were collected on a VG Quattro MS/MS spectrometer and

HP5989A mass spectrometer respectively. ^{1}H NMR and ^{13}C NMR were performed on Bruker AMX-600 spectrometer in $CDCl_3$. HPLC was carried out with Beckman-344 HPLC instrument using a Spherisob-C column (10 mm × 300 mm) equipped with ALTEX-156 refractive index detector.

Plant Material

Seeds of *Annona atemoya* were collected in Guangzhou, China, in 1996. The material was authenticated by Professor Bing Tao Li at South China Agriculture University. A voucher specimen of the seed is preserved in South China Institute of Botany, Chinese Academy of Sciences.

Extraction and Isolation

The powdered seeds (500 g) were defatted with hexane and then percolated repeatedly with 95% ethanol. The ethanol extracts were evaporated *in vacuo* to give a syrup, which was again extracted with acetone to give acetone soluble portion I (28 g) and residue II (22 g). Potion I was extracted with $CHCl_3$, then the concentrated $CHCl_3$ extract (8.5 g) was chromatographed over silica gel column (400 mesh, 250 g) using gradients of (A) hexane/acetone (7 : 3), (B) hexane/acetone (1 : 1) and (C) acetone successively, each fraction volume was 100 mL. Fractions 1 – 19 were collected using A as eluant, fractions 20 – 32 were collected using B as eluant, and fractions 33 – 36 using C as eluant. The fractions 20 – 32 (950 mg) was subjected to preparative TLC (ethyl acetate/hexane 3 : 2) to give a crude product (205 mg). Further separation was achieved by HPLC to yield compound **1** (20.4 mg).

Portion II was chromatographed over silica gel column eluted with ethyl acetate/$CHCl_3$ (4:1) to give compound **2** as a crystal.

Preparation of TMS Derivative (1a)

Compound **1** (ca. 0.2 mg) was treated with *N,O*-bis(trimethylsily) acetamide (20 uL) and pyridine (2 uL) and heated at 70°C for 30 min to yield the tetra-TMS derivative. EIMS fragmentaion was shown in Figure 2.

Atemoyacin E (1)

Yellow waxy solid. m.p. 51 – 52°C; $[\alpha]_D = +21.8$ (c 0.22, MeOH), UV(MeOH) λ_{max} : 208 nm ($\log\varepsilon = 4.04$); IR ν_{max} (KBr) cm^{-1} : 3425, 2925,

2854, 1748, 1466, 1375, 1321, 1204, 1071, 1029, 756; HRFABMS for $C_{37}H_{66}O_8Na$ $[M+Na]^+$ calcd 661.4650 found 661.4636; ESIMS m/z : 662 $[M+H+Na]^+$; ^1H NMR (600 MHz, $CDCl_3$), ^{13}C NMR (150 MHz, $CDCl_3$) and EIMS: see Table I and Figure 2.

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