Chinese Chemical Letters Vol. 11, No. 3, pp. 239–242, 2000

Muricatenol, a Linear Acetogenin from *Annona muricata* (Annonaceae)

De Yu LI, Jing Guang YU*, Xiu Zhen LUO, Lan SUN, Shi Lin YANG

Institute of Medicinal Plant Development, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100094

Abstract: Muricatenol **1**, a new acetogenin, has been isolated from the seeds of *Annona muricata* L.. Compound **1** is a C_{37} acetogenin without any THF rings, with four hydroxyls and one double bond in the long aliphatic chain. The hydroxyls of **1** are located at C-4, C-10, C-18 and C-19, respectively. The vicinal diol at C-18/C-19 is *threo*-configuration, and the double bond at C-14/C-15 is *cis*-configuration.

Keywords: *Annona muricata*, Annonaceae, acetogenins, muricatenol.

Annonaceous acetogenins (polyketides) are a group of extensively investigated natural compounds possessing antitumor, antiparasitic and pesticidal activities. Over 350 acetogenins have been isolated and most of them have one to three tetrahydrofuran (THF) cores, several hydroxyls and a terminal γ-lactone ring. As part of our investigation of the title species, we have reported four new C_{35} acetogenins: muricatalin[1], muricatalicin[2], annonacin-B[3] and murihexol **2**[4] and four known acetogenins: annonacin, annonacin-A, annonacin-10-one and donhexocin **3**[4]. Among them, murihexol **2** and donhexocin **3** are two non-THF acetogenins (**Figure 2**). Here we report a new C_{37} non-THF acetogenin, muricatenol **1**, which lacks THF cores and expoxide rings, only possessing four hydroxyls and one double bond in the long aliphatic chain, as shown in **Figure 1**.

Figure 1. The structure of muricatenol **1**

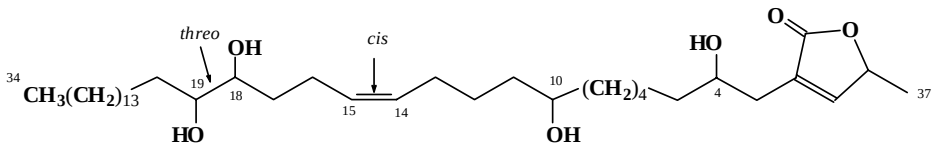
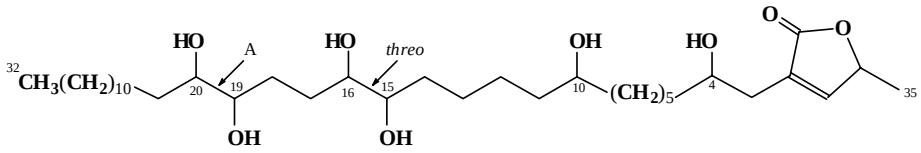


Figure 2. The structures of **2, 3**



Murihexol 2: A=*erythro*, **Donhexocin 3**: A=*threo*

Muricatenol **1** was isolated as white crystals, mp. 50-53°C. The molecular formula was established to be $C_{37}H_{68}O_6$ by the peak of HRFAB-MS at *m*/*z* 609.4993 $[M+H]^+$(calcd. 609.5076). It showed IR absorption bands at 3400 cm^{-1} (OH) and 1745 cm^{-1} (C=O), ^1H NMR at δ_H 7.19 (1H, d, J=1.4Hz), 5.07 (1H, qd, J=7.0, 1.4Hz) and 1.44 (3H, d, J=7.0Hz) and ^{13}C NMR at δ_C 174.60 (C=O), 151.88, 131.05 (C=C), 78.02 (C-O) and 19.1 (CH_3). These data supported the presence of an α,β-unsaturated γ-methyl γ-lactone moiety in an annonacin-type acetogenin[5]. Compound **1** exhibited five carbon signals of C-O bonds in ^{13}C NMR and five proton signals of H-C-O bonds in the ^1H NMR spectrum. These included the signals of the lactone moiety at δ_C 78.02 and δ_H 5.07, four signals of hydroxylated methines at δ_C 69.93, 71.84, 74.18 and 74.48, δ_H 3.85 (1H), 3.59 (1H) and 3.43 (2H), respectively. The EI-MS data also supported there were four hydroxyls in **1**. The non-equivalent signals of H-3a and H-3b of **1** at δ_H 2.41 (1H, ddt, J=15.0, 8.0, 1.4Hz) and 2.54 (1H, ddt, J=15.0, 4.4, 1.4Hz) in the ^1H NMR suggested the presence of a C-4 OH[5]. Lack of signals in the δ_C 79.00-82.00 region of ^{13}C NMR in **1** strongly indicated the absence of any THF cores in the molecule. ^1H NMR at δ_H 5.42 (1H, dt, J=11.0,7.0Hz), 5.37 (1H, dt, J=11.0, 7.0Hz) and ^{13}C NMR at δ_C 131.05, 128.84 supported the presence of an isolated double bond in **1** (**Table 1**). The diagnostic EI fragment ions in the mass spectrum and HRMS analysis showed the hydroxyls were located at C-10 (241→223→205), C-18 (337→319→301) and the isolated double bond was between them. ^1H NMR at δ_H 3.43 (2H, m) and ^{13}C NMR at δ_C 74.48, 74.18 showed there were one vicinal diol in **1** [4], with the HRMS data, it should be located at C-18/C-19. The ^{13}C NMR and ^1H NMR signals at δ_C 74.48, 74.18 and δ_H 3.43 (2H) representing the vicinal diol at C-18/C-19 must be in *threo*-configuration. The diagnostic ions in the EI mass spectrum showed the double bond was located at C-14/C-15 (339→321→303 and 269→251→233, double bonds often had β–homolysis). The ^1H NMR signals at δ_H 5.42 (1H, dt, J=11.0, 7.0Hz), 5.37 (1H, dt, J=11.0, 7.0Hz) representing the double bond at C-14/C-15 must be in *cis*-form (**Table 2**, **Figure 3**). From all these data, **1** has four hydroxyls, located at C-4, C-10, C-18 and C-19 respectively, one isolated double bond located at C-14/C-15, and was named muricatenol.

Table 1. NMR data for compound **1** (125/500MHz, $CDCl_3$)

C/H	^{13}C	^{1}H (J in Hz)
1	174.60	--
2	131.05	--
3a	33.11	2.41 ddt (15.0, 8.0, 1.4)
3b	--	2.54 ddt (15.0, 4.4, 1.4)
4	69.93	3.85 m
10	71.84	3.59 m
14	131.01	5.42 dt (11.0, 7.0)
15	128.84	5.37 dt (11.0, 7.0)
18	74.48	3.43 m
19	74.18	3.43 m
34	14.12	0.88 t (7.0)
35	151.88	7.19 d (1.4)
36	78.02	5.07 qd (7.0, 1.4)
37	19.11	1.44 d (7.0)
CH_2[#]	22-37	1.26-1.65 m

[#] These included signals of carbons and protons at C-5 to C-9, C-11 to C-13, C-16 to C-17, and C-20 to C-33.

Figure 2. Diagnostic fragment ions of muricatenol **1**

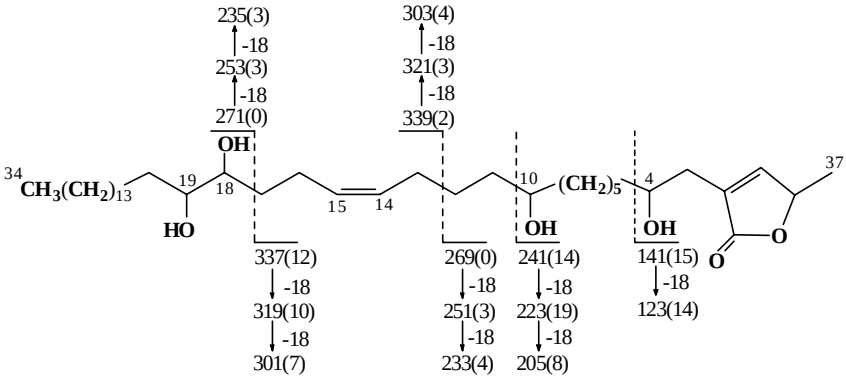


Table 2. High resolution mass spectral data and elemental compositions of muricatenol **1**

m/z of ions	Compositions
C-17/18	
337.2379	$C_{20}H_{33}O_4$
319.2270	$C_{20}H_{31}O_3$
301.2162	$C_{20}H_{29}O_2$
C-10/11	
241.1444	$C_{13}H_{21}O_4$
223.1331	$C_{13}H_{19}O_3$
205.1227	$C_{13}H_{17}O_2$

Acknowledgment

This project was supported by the National Natural Science Foundation

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Received 13 September 1999