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Mitregenin, a New Annonaceous Acetogenin from *Mitrephora maingayi*

Qiang Zhang, Ying-Tong Di, Hong-Ping He, Shun-Lin Li and Xiao-Jiang Hao*

State Key Laboratory of Phytochemistry and Plant Resources in West China, Kunming Institute of Botany, Chinese Academy of Sciences, Kunming PRC, 650204

Haoxj@mail.kib.ac.cn

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From *Mitrephora maingayi*, a new C_{21}-type Annonaceous acetogenin (**1**) has been isolated, along with a biogenetically related known compound, oropheic acid (**2**). Their structures were elucidated on the basis of extensive spectroscopic analysis. The insecticidal activity of **1** was also assessed.

Keywords: *Mitrephora maingayi*, Annonaceous acetogenin, mitregenin.

Mitrephora (Annonaceae) is a large genus of approximately 40 species, which are distributed mainly in tropical Asia and Oceania. Among them, *M. maingayi* is a tree growing in deciduous forest in Thailand and southern China [1a]. Previous phytochemical investigations of the plant revealed the presence of terpenoids [1a], 5-oxonorporphines [1b], and an alkaloid [1c]. The present studies on twigs and leaves led to the isolation of a new C_{21}-type acetogenin, mitregenin (**1**), together with the related known compound, oropheic acid (**2**) [1d].

Mitregenin (**1**) showed a pseudomolecular ion peak at *m/z* 351.1923 ($[M+Na]^+$, calcd. 351.1936), which indicated the molecular formula $C_{21}H_{28}O_3$ with eight degrees of unsaturation. IR signals indicated the presence of hydroxyl (3425 cm^{-1}), a terminal double bond (2931 cm^{-1}), triple bonds (2222 and 2138 cm^{-1}) and a lactone (1761 cm^{-1}) group. ^{13}C NMR and DEPT (Table 1) revealed 11 methylenes, 5 methines and 5 quaternary carbons. Combined analysis of chemical shifts and IR signals revealed two double bonds, two triple bonds and an ester group, which accounted for seven degrees of unsaturation; the remaining one indicated that **1** should possess a ring in its skeleton. Extensive analysis of the 2D NMR spectra (HSQC, ^1H–^1H COSY and HMBC) revealed the framework of **1**. All protons directly bonded to carbon atoms were assigned from the HSQC spectrum. The interaction pairs in ^1H-^1H COSY provided fragments **a** (C-2 to C-19 and C-19 to C-21), **b** (C-6 to C-8) and **c** (C-13 to C-18), as shown in Figure 1. However, the

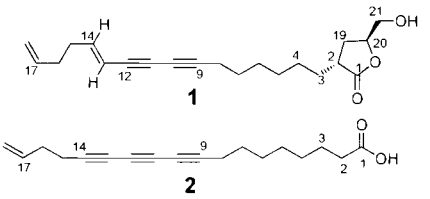

Table 1: ^1H and ^{13}C NMR data of compound **1** (in $CDCl_3$).

	δ_H (*J* in Hz)	δ_C		δ_H (*J* in Hz)	δ_C
1		180.2	**12**		73.6
2	2.65 d (8.6)	39.4	**13**	5.45 d (15.8)	108.9
3a	1.33 m	30.9	**14**	6.20 dt (15.8, 6.8)	146.9
3b	1.76 m		**15**	2.16 q (7.5)	32.2
4	1.33 m	28.6	**16**	2.09 q (7.5)	32.4
5	1.33 m	28.3	**17**	5.71 m	137.0
			18a	4.94 d (11.0)	115.1
6	1.35 m	27.9	**18b**	4.98 d (17.0)	
7	1.47 m	26.8	**19a**	1.75 m	29.4
8	2.26 t (6.0)	19.2	**19b**	1.94 m	
9		83.4	**20**	4.53 m	78.8
10		65.1	**21a**	3.57 dd (12.5, 4.0)	64.0
11		72.9	**21b**	3.79 d (11.0)	

overlapped COSY cross-peaks (δ_H 1.33~1.38) for the methylenes at C-3, C-4 and C-5 were difficult to differentiate. Detailed HMBC analysis overcame the difficulty and established the connections of the three substructures and the other atoms. The HMBC correlations from H-2, H-19 and H-20 to C-1 revealed a γ-lactone ring. The HMBC correlations of H-2/C-3, H-2/C-4, H-6/C-4 and H-7/C-5 confirmed that the connection of the moieties **a** and **b** via the carbonic chain C-3 to C-5. Furthermore, moieties **b** and **c** were linked through two triple bonds on the basis of the HMBC correlations of H-7, 8, 13, 14 with the sp hybrid

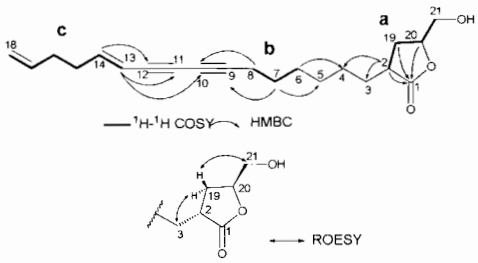

Figure 1: Selected 2D NMR correlations of **1**.

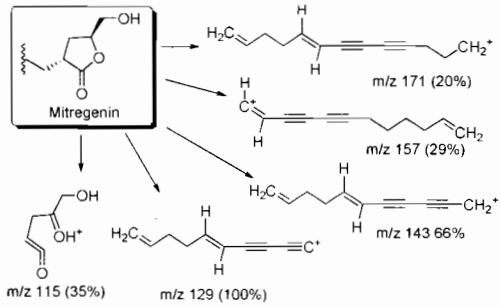

Figure 2: The EI fragment ions of **1**.

carbons (C-9, 10, 11, 12). In addition, the coupling constant of 15.8 Hz between H-13 and H-14 indicated the *trans* configuration of the double bond between C-13 and C-14. Thus the planar structure was elucidated as depicted. The relative configuration of C-2 and C-20 was determined by ROESY correlations, as shown in Figure 1. The interaction pairs of H-3/H_a-19 and H_a-21/H_b-19 indicated the *anti* configuration of the aliphatic chain and the hydroxymethyl at C-21. The latter group was arbitrarily assigned with a β-orientation.

Annonaceous acetogenins are notable for their diverse bioactivities, including insecticidal effects [2]. Due to the instability of **2**, only **1** was evaluated for insecticidal activity against *Plutella xylostella* on an artificial diet (500 ppm) and *Heliothis virescens* on cotton (1000 ppm). No significant mortality was detected.

Experimental

General: NMR, Bruker (AM-400, DRX-500) spectrometer; ESIMS and HRESIMS, API QSTAR spectrometer; EIMS, Finnigan Trace DSQ spectrometer; Optical rotation, Perkin-Elmer model 241 polarimeter; IR, Bio-Rad FTS-135 spectrometer with a KBr disk; CC, silica gel (90–150 μm; Qingdao Marine Chemical Inc. Inc. China) and Sephadex LH-20 (40–70 μm; Amersham Pharmacia Biotech AB, Uppsala, Sweden); Precoated silica gel GF_{254} and HF_{254} plates (Qingdao Marine Chemical Inc. Qingdao, China) were used for TLC.

Plant material: The twigs and leaves of *M. maingayi* were collected from Xishuangbanna, Yunnan Province, PRC in October 2007. The plant was identified by Prof. Jingyun Cui of the Xishuangbanna Tropical Botanical Garden, Chinese Academy of Sciences. A voucher specimen was deposited at the Kunming Institute of Botany, Kunming, PRC.

Extraction and isolation: The air-dried powdered plant material (20 kg) was extracted with MeOH 3 times at room temperature. After evaporation of the solvent, the residue was suspended in water and extracted with light petroleum. The light petroleum fraction was separated over a silica gel column eluted by light petroleum/acetone (1:0 - 0:1) to give 5 fractions. The second and third fractions were further chromatographed on silica gel and Sephadex LH-20 repeatedly to afford **1** (210 mg) and oropheic acid **2** (43 mg) [1d], respectively. However, **2** appeared to be rather unstable, decomposing into a blue mixture insoluble in $CHCl_3$ and MeOH.

Mitregenin

Colorless oil.
$[\alpha]_D^{24}$: −13.1 (*c* 0.59, $CHCl_3$).
IR (KBr): 3425, 2931, 2222, 2138, 1761, 1172 cm^{-1}.
UV/Vis λ_{max} (MeOH): 283.4, 267.2, 253.2 nm.
^{1}H and ^{13}C NMR ($CDCl_3$): Table 1
MS (EI, 70 eV): *m/z* (%) = 171 (20), 157 (29), 143 (66), 129 (100), 115 (35).
HRESIMS: *m/z* 351.1923 ([M + Na]$^+$, calcd for $C_{21}H_{28}O_3Na$: 351.1936.)

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