

## Clausenolide-1-methyl ether from *Clausena heptaphylla* W&A

[Clausenolido-1-metil éter de *Clausena heptaphylla* W & A]

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### Abstract

From the stem bark of *Clausena heptaphylla*, the limonoid clausenolide-1-methyl ether (**1**) was isolated. The structure of the compound was elucidated by extensive spectroscopic studies, including 2D NMR and MS measurements and by comparison with spectroscopic and physical data from the literature. This is the first report of occurrence of clausenolide-1-methyl ether (**1**) in *Clausena heptaphylla*.

**Keywords:** *Clausena heptaphylla*, clausenolide-1-methyl ether

### Resumen

El limonoide clausenolido-1-metil eter (**1**) fue aislado de corteza de *Clausena heptaphylla*. La estructura del compuesto fue determinada por métodos espectroscópicos, incluyendo 2D RMN, espectrometría de masas (EM) y comparación de los datos espectroscópicos y constantes físicas con los publicados en la literatura. Este es el primer informe del aislamiento de clausenolido-1-metil eter (**1**) de *Clausena heptaphylla*.

**Palabras Clave:** *Clausena heptaphylla*, clausenolido-1-metil eter

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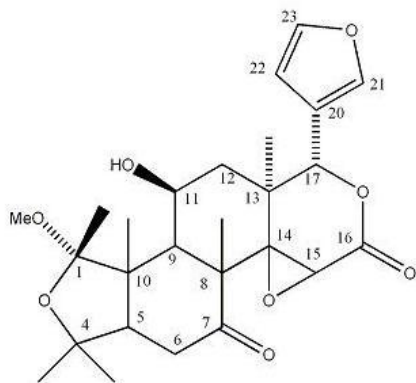
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## INTRODUCTION

*Clausena heptaphylla* W & A (Bengali name: Panbilash, Karanphul, Pomkaphur, Family: Rutaceae) is a small bushy shrub that is distributed throughout Bangladesh, India and other parts of south east Asia (Haque 1986). The plant is reported to have antiseptic property. *Clausena* species are known to be useful in paralysis, ulcerated nose, headache, muscular pain and malarial fever. They are also reputed as diuretic, astringent, insecticide, tonic and vermifuge (Yusuf *et al.*, 1994). Previous phytochemical investigations of *Clausena* species led to the isolation of amides (Riemer *et al.*, 1997), limonoids (Ngadjui *et al.*, 1989a; Thuy *et al.*, 1999), carbazole and quinolone alkaloids (Ngadjui *et al.*, 1989b; Wu *et al.*, 1996; Begum *et al.*, 2008), coumarins (Thuy *et al.*, 1999; Huang *et al.*, 1997), terpenes (He *et al.*, 2002; Sohrab *et al.*, 1999), cyclopeptide (Wang *et al.*, 2005) and carboxamide (Milner *et al.*, 1996). As a part of our work on Bangladeshi medicinal plants (Ara *et al.*, 2006; Islam *et al.*, 2009, Jahan *et al.*, 2010.), we investigated *C. heptaphylla* and isolated a limonoid, clausenolide-1-methyl ether (**1**) which is the first report of its occurrence from this plant.



(1)

## EXPERIMENTALS AND METHODS

**General Experimental Procedures:** NMR spectra (both 1D and 2D) were obtained on a Ultra Shield Bruker DPX 400 NMR instrument, using the residual solvent peaks ( $\text{CDCl}_3$ ) as internal standard. Mass spectrum was obtained with a LCT premier KD146 TOF analyzer using positive mode ESI technique.

## Plant material

The stem bark of *C. heptaphylla* was collected from Barisal in May 2005 and was identified by Dr. Mahbuba Khanam, Director in charge, Bangladesh National Herbarium, Ministry of Environment and Forest, Dhaka, Bangladesh where a voucher specimen (accession number DACD-31,252) has been maintained for this collection.

## Extraction and isolation

The powdered stem bark (210 g) of *C. heptaphylla* was soaked in 800 ml MeOH, for 5 days and then filtered and concentrated using rotary evaporator at low temperature and reduced pressure. A portion (5 gm) of the concentrated methanol extract was fractionated by the modified Kupchan (VanWagenen *et al.*, 1993) procedure into *n*-hexane, carbon tetrachloride, chloroform and aqueous soluble fractions. Evaporation of solvents from the extractives afforded *n*-hexane (0.2 g), carbon tetrachloride (1.94 g), chloroform (1.85 g) and aqueous (1.00 g) soluble materials. The chloroform soluble material was subjected to vacuum liquid chromatography (VLC) over silica gel 60H, and the column was eluted with *n*-hexane-EtOAc mixtures of increasing polarity yielding 20 fractions, each of 100 ml. VLC fractions eluted with 20 % ethyl acetate in hexane afforded compound **1** (12.1 mg) as crystalline white mass.

## RESULTS

**Clausenolide-1-methyl ether (1):** White crystalline mass;  $^1\text{H NMR}$  (400 MHz,  $\text{CDCl}_3$ ),  $\delta$ . 1.10, 1.14, 1.22, 1.43, 1.45, 1.54 (each 3H, s), 2.33 (1H, dd,  $J=14.0$ , 3.4 Hz,  $\text{H}_{\alpha-6}$ ), 2.62 (1H, dd,  $J=16.0$ , 3.4 Hz, H-5), 2.72 (1H, br.s, H-9), 2.87 (1H, dd,  $J=16.0$ , 14.0 Hz,  $\text{H}_{\beta-6}$ ), 3.98 (1H, s, H-15), 4.51 (1H, br.s, H-11), 5.54 (1H, s, H-17), 6.35 (1H, d,  $J=1.5$  Hz, H-22), 7.38 (1H, s, H-21), 7.40 (1H, d,  $J=1.5$  Hz, H-23), -OMe (3.22);  $^{13}\text{C NMR}$ :  $\delta$  108.5 (C-1), 79.9 (C-4), 54.7 (C-5), 37.0 (C-6), 208.1 (C-7), 50.6 (C-8), 44.70 (C-9), 51.0 (C-10), 67.1 (C-11), 43.4 (C-12), 41.0 (C-13), 65.7 (C-14), 54.5 (C-15), 167.2 (C-16), 78.3 (C-17), 120.3 (C-20), 141.1 (C-21), 109.9 (C-22), 143.0 (C-23), 30.8, 23.3, 20.2, 19.3, 18.0, 17.3 (6 $\times$ C-Me), 55.72 (OMe);  $\text{C}_{26}\text{H}_{34}\text{O}_8$  (ESI-TOFMS:  $[\text{M}+\text{H}]^+$   $m/z$  475.2010).

## DISCUSSION

The high resolution electro-spray ionization (ESI-TOF) mass spectrum of compound **1** displayed the pseudo-molecular ion peak  $[\text{M}+\text{H}]^+$  at  $m/z$  475.2010 suggesting a molecular formula  $\text{C}_{26}\text{H}_{34}\text{O}_8$ . The  $^{13}\text{C NMR}$  spectrum of this compound displayed 26 carbon

resonances consistent with the molecular formula and also revealed similarity in resonances typical of limonoids (Kipassa *et al.*, 2008). The <sup>1</sup>H NMR spectrum of compound **1** showed six three proton singlets at  $\delta$  1.10, 1.14, 1.22, 1.43, 1.45 and 1.54, which were assigned to the methyl groups at C-13, C-4 (2 x CH<sub>3</sub>), C-8, C-1 and C-10 respectively in a limonoid-type carbon skeleton. Also showed, the presence of a sharp three proton singlet at  $\delta$  3.22 ( $\delta_c$  55.72) which suggested the presence of one OCH<sub>3</sub> group. In the HMBC spectrum, the methoxy group at  $\delta$  3.22 showed connectivity (<sup>3</sup>J) with C-1 ( $\delta$  108.5). Thus the methyl group was linked to C-1. A broad singlet at  $\delta$  4.51 and a sharp singlet at  $\delta$  3.98, each integrated for one proton, were ascribed to the equatorial protons H-11 and H-15, respectively. The spectrum also exhibited signals characteristic of a  $\beta$ -substituted furan, with resonances at  $\delta$  6.35, 7.38 and 7.40 assignable to H-22, H-21 and H-23, respectively. The one proton singlet at  $\delta$  5.54 was attributed to H-17, the attachment site of the furan moiety. On this basis, compound **1** was characterized as clausenolide-1-methyl ether, a limonoid previously reported from *C. excavate* (Wu *et al.*, 1992). The identity of this compound was further substantiated by comparison with spectroscopic and physical data from the literature (Wu *et al.*, 1992). This is the first report of its occurrence in *C. heptaphylla*.

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