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Chinese Chemical Letters 19 (2008) 65–67
CHINESE CHEMICAL LETTERS
www.elsevier.com/locate/cclet

A new pyrrolidone derivative from *Pistacia chinensis*

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Received 4 July 2007

Abstract

A new *N*-phenyl-pyrrolidone derivative had been isolated from *Pistacia chinesis* Bunge. Its structure was elucidated as 4-hydroxy-5-(2-oxo-1-pyrrolidinyl)-benzoic acid, named pistaciamide on the basis of the 1D-NMR, DEPT, HMQC and HMBC spectroscopic techniques.

Keywords: *Pistacia chinensis*; 4-Hydroxy-5-(2-oxo-1-pyrrolidinyl)-benzoic acid; Pistaciamide; Pyrrolidone derivative

Pistacia chinensis Bunge. (Anacardiaceae), widely distributed in China, is well-known as a landscaping and street trees. Its tender burgeon is used as an edible wild vegetable and tea in Chinese folk for its function of clearing away heat and toxic material; and its seeds used as an oil material [1]. Up to now, the chemical constituents of this plant had been fastened mainly on flavonoids and phenolic compounds [1–3]. Our investigation on this plant led to the isolation of a new *N*-phenylpyrrolidone derivative. This paper reports the isolation and structural elucidation of the new compound.

The fresh tender burgeon and anthotaxy (10 kg, collected from Yuanjiang, Yunnan Province, April, 2005) was extracted exhaustively with 90% EtOH at room temperature. The EtOH extract was evaporated at 45 °C to yield a black residue (743 g). The residue was suspended in H_2O and extracted with petroleum ether, EtOAc, *n*-butanol, respectively. The EtOAc extract (374 g) was subjected to silica gel column chromatography with $CHCl_3$–MeOH (gradiently) as eluent to give fractions *I–V*. Fraction II (10% MeOH/$CHCl_3$) was purified by Sephadex LH-20 column chromatography eluted with MeOH/H_2O gradiently from 25:100 to 100:20. The fraction was eluted with MeOH/H_2O (1:1) to afford compound **1** (10 mg).

Compound **1** was obtained as colorless needle crystals (MeOH), m.p. 218–220 °C. UV: λ_{max}^{MeOH} (log ε) 223 (4.18) nm. The EI-MS showed a molecular ion peak at *m/z* 221. The molecular formula of it was assigned as $C_{11}H_{11}O_4N$ by the HR-ESI-MS (*m/z* = 222.0766 $[M + 1]^+$; calcd. 222.0766). The IR spectrum (KBr) revealed the presence of –COOH (3500–2500 cm^{-1}, 1419 cm^{-1}, 1311 cm^{-1}, 1290 cm^{-1}), –OH group (3442 cm^{-1}), –C=O (1685 cm^{-1}, 1637 cm^{-1}) and aromatic ring (1589 cm^{-1} and 1493 cm^{-1}). The ^{13}C NMR and DEPT spectra displayed eleven C-atom resonances, including two –C=O groups at δ175.5 (s, C-2′), 169.0 (s, C-7) ppm, a trisubstituted phenyl at

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1001-8417/$ – see front matter
doi:10.1016/j.cclet.2007.10.037

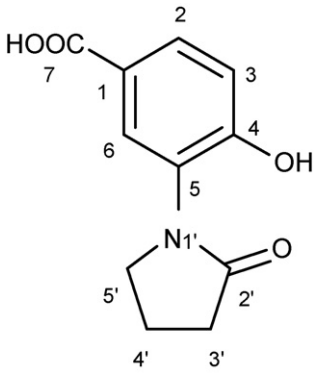

Fig. 1. Structure of compound 1.

δ157.9 (s, C-4), 130.7 (d, C-2), 130.4 (d, C-6), 127.5 (s, C-1), 123.6 (s, C-5), 117.7 (d, C-3) ppm, and three $-CH_2$ at δ 49.9 (t, C-5′), 31.6 (t, C-3′) and 19.7 (t, C-4′) ppm. The ^1H NMR spectrum indicated three $-CH_2$ at δ_H 1.90 (m, 2H, H-4′), 2.45 (t, 2H, H-3′), 3.80 (t, 2H, H-5′) ppm, and three aromatic protons at δ_H 7.29 (d, 1H, H-3), 8.30 (dd, 1H, H-2) and 8.53 (d, 1H, H-6) ppm. These observations, in combination with the molecular formula, indicated the presences of phenyl and pyrrolidinyl moieties, two –C=O groups and one hydroxyl group (Fig. 1).

Extensive 2D-NMR (HMQC and HMBC) experiments allowed us to define the molecular connectivity. The connections of protons and carbons were unambiguously assigned by the HMQC experiment (see Table 1). The ^{13}C–^1H long range couplings (^2J and ^3J) in the HMBC spectrum (see Fig. 2) gave the following results: the strong cross-peaks from δ_C 169.0 (C-7) to δ_H 8.53 (H-6) and δ_H 8.30 (H-2) suggested that the carboxyl group is connected directly with phenyl group with its *ortho* positions unsubstituted. The correlations from proton at δ_H 7.29 (H-3) to δ_C 127.5 (C-1), 123.6 (C-5), from δ_H 8.30 (H-2) to δ_C 157.9 (C-4), 130.4 (C-6) and 169.0 (C-7), and from the proton at δ_H 8.53 (H-6) to δ_C 157.9 (C-4), 130.7 (C-2) and 169.0 (C-7) suggested that *N*-pyrrolidinyl and hydroxyl located in the *meta* and *para* positions of the carboxyl group, respectively. Furthermore, HMBC correlation of δ_H 2.45 (H-3′) with δ_C 19.7 (C-4′), 49.9 (C-5′) and 175.5 (C-2′), δ_H 1.90 (H-4′) with δ_C 31.6 (C-3′), 49.9 (C-5′) and 175.5 (C-2′), and δ_H 3.80 (H-5′) with δ_C 19.7 (C-4′), 31.6 (C-3′), 175.5 (C-2′) indicated the existence of 2-pyrrolidonyl moiety. Thus, the structure of compound **1**, HMBC correlation of it shown in Fig. 2; the data of ^{13}C, ^1H NMR, HMQC and HMBC see Table 1, was identified as 4-hydroxy-5-(2-oxo-1- pyrrolidinyl)-benzoic acid, named pistaciamide.

Pyrrolidone derivatives have an important value in chemical industry as an intermediate. Etiracetam and Pramiracetam, as a synthesized drug of pyrrolidone, were used to treat brain dementia and brain concussion syndrome

Table 1
^1H, ^{13}C NMR data and HMBC correlations of compound **1**

Position	HMQC		HMBC (H → C)
	δ_C	δ_H	
1	127.5s		
2	130.7d	8.30 (1H, dd, 8.4, 1.9)	C-4, C-6, C-7
3	117.7d	7.29 (1H, d, 8.4)	C-1, C-4, C-5
4	157.9s		
5	123.6s		
6	130.4d	8.53 (1H, d, 1.9)	C-2, C-4, C-7
7	169.0s		
2′	175.5s		
3′	31.6t	2.45 (2H, t, 8.0)	C-2′, C-4′, C-5′
4′	19.7t	1.90 (2H, m)	C-2′, C-3′, C-5′
5′	49.9t	3.80 (2H, t, 6.9)	C-2′, C-3′, C-4′

The NMR data were recorded on Bruker AV-400 (pyridine-d^5, TMS, δppm, *J* in Hz).

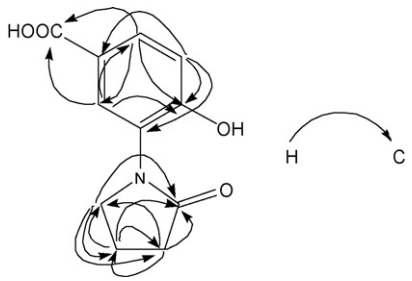

Fig. 2. Key HMBC correlations of compound 1.

[4,5]. Clausenamide, which was isolated from Chinese traditional medicine ‘‘huang pi’’, was an important medicine for the treatment of brain dysfunction [6]. The biological activities of this compound need to be further investigated.

Acknowledgment

This work was supported by the Natural Science Foundation of Yunnan Province of China (No. 2005B0049M).

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