

## Gymnastone, A New Benzofuran Derivative from *Gymnaster koraiensis*

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A new benzofuran derivative, named gymnastone [5-hydroxy-6-acetyl-2-(2-propane-1,2,3-triol)-benzofuran (1)], was isolated from the aerial part of *Gymnaster koraiensis*, together with viscidone (2) by repeated column chromatography. The structures of both compounds were identified by physico-chemical and spectral analysis including COSY, HMQC, and HMBC experiments.

**Keywords:** *Gymnaster koraiensis*, Asteraceae, Gymnastone, Viscidone

### INTRODUCTION

*Gymnaster koraiensis* (Nakai) Kitamura (Asteraceae) is an endemic species to Korea and much cultivated for gardening by its beautiful flowers. Previously, we reported eight polyacetylenes from the CH<sub>2</sub>Cl<sub>2</sub> fraction of an 80% EtOH extract of the roots of *G. koraiensis*, which showed significant cytotoxicity against L1210 tumor cells with ED<sub>50</sub> values of 0.12-3.28 µg/mL (Jung *et al.*, 2002). And also we isolated two new polyacetylene glycosides from the BuOH-soluble fraction of the roots of *G. koraiensis* (Park *et al.*, 2002). As a part of our continuing studies to discover pharmacologically active constituents from this plant, we have isolated a new and a known benzofuran derivatives, called gymnastone (1) and viscidone (2), from the MeOH extract of the aerial part of *G. koraiensis*. This paper describes the isolation and structure elucidation of two benzofuran derivatives from *G. koraiensis*.

### MATERIALS AND METHODS

#### General experiment procedure

Melting points were measured using a Yanagimoto micro hot-stage melting point apparatus and were uncorrected. IR spectra were obtained from a JASCO 100 IR spectrophotometer; UV spectra from a JASCO V-550 UV/VIS

spectrometer; <sup>1</sup>H- and <sup>13</sup>C-NMR spectra from a BRUKER DRX-300 and -600 NMR spectrometer; and FAB-MS spectra from a JEOL JMS-HX/HX 110A tandem mass spectrometer.

#### Plant materials

The aerial parts of *G. koraiensis* were collected in a plant garden at Chungnam National University (Korea) in October 2001 and identified by Prof. Young Ho Kim. A voucher specimen (CNU 01004) was deposited at the Herbarium of College of Pharmacy, Chungnam National University.

#### Extraction and isolation

The aerial parts of *G. koraiensis* (2.9 kg) were dried at room temperature, powdered, and extracted with hot MeOH (6 L × 3 times). The MeOH extract (162 g) was then suspended in water (2 L) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (700 mL × 3 times) and BuOH (700 mL × 3 times), successively. The BuOH fraction (78.0 g) was subjected on a silica-gel column (500 g, 8 × 20 cm) with CH<sub>2</sub>Cl<sub>2</sub>-MeOH (5:1 v/v, 9.0 L) as the eluent to afford four fractions (Fr. A~D). Compound 1 (4.5 mg) was obtained from Fr. C using a Sephadex LH 20 column (80 g, 2.5 × 50 cm) eluted by MeOH-H<sub>2</sub>O (1:1, 800 mL). Fr. A was followed a silica-gel column (120 g, 2 × 40 cm) eluted with hexane-CHCl<sub>3</sub>-EtOAc (2:1:1, 2.0 L) to yield compound 2 (11.9 mg) as yellow powder.

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**Gymnastone (1)**

Yellow amorphous powder; mp 179-180 °C; IR  $\nu_{\max}$  (KBr): 1730 (C=O), 1590, 1480 and 1420 (C=C ring)  $\text{cm}^{-1}$ ; FAB-MS:  $m/z$  267 [M+H]<sup>+</sup>; HR-FAB-MS:  $m/z$  267.0869 (Calcd. 267.0872 for C<sub>13</sub>H<sub>15</sub>O<sub>6</sub>); <sup>1</sup>H-NMR (600 MHz, CD<sub>3</sub>OD) and <sup>13</sup>C-NMR (150 MHz, CD<sub>3</sub>OD): see Table I.

**Viscidone (2)**

Yellow amorphous powder; mp 78-80 °C; [ $\alpha$ ]<sub>D</sub><sup>25</sup> + 68.9° (c 0.5, CHCl<sub>3</sub>); FAB-MS:  $m/z$  235 [M+H]<sup>+</sup>; <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) and <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>): see Table I.

**RESULTS AND DISCUSSION**

Compound **1** was obtained as a yellow amorphous powder. The HR-FAB-MS spectrum of **1** revealed a [M+H]<sup>+</sup> peak at  $m/z$  267.0869 corresponding to a molecular formula C<sub>13</sub>H<sub>15</sub>O<sub>6</sub>. The IR spectrum of **1** revealed a carbonyl group at 1730  $\text{cm}^{-1}$ , absorption bands characteristic for the aromatic ring at 1590, 1480 and 1420  $\text{cm}^{-1}$ . In the <sup>1</sup>H-NMR spectrum, an acetyl group ( $\delta$  2.67, 3H, s), three aromatic singlet peaks at  $\delta$  7.97, 6.99, 6.75 (each 1H, s), and two hydroxy methylene peaks ( $\delta$  3.88, 4H, dd,  $J$  = 11.1 and 16.2 Hz) were recognized. The <sup>13</sup>C-NMR spectrum of **1** showed the presence of an acetyl group ( $\delta$  25.9 and 204.8), six aromatic carbon signals ( $\delta$  107.1-158.1), furan ring moiety ( $\delta$  165.8 and 104.3), and two oxygen attached carbon signals ( $\delta$  75.5 and 64.8). The HMBC correlation showed the coupling between methyl protons H-11 ( $\delta$  2.67) and carbons C-10 ( $\delta$  204.8)/C-6 ( $\delta$  116.4), between proton H-3 ( $\delta$  6.75) and carbons C-2 ( $\delta$  165.8)/C-4 ( $\delta$  107.1)/C-8 ( $\delta$  148.5)/C-9 ( $\delta$  136.8), and between methylene

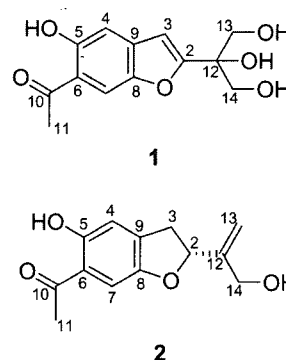


Fig. 1. Structures of compounds isolated from *G. koraiensis*

protons H-13 and H-14 ( $\delta$  3.88) and quaternary carbons C-12 ( $\delta$  75.5)/C-2 ( $\delta$  165.8) (see Fig. 2). Those characteristics suggested the *p*-hydroxyacetophenone having benzofuran structure (Ngo and Pham, 1981; Bohlmann *et al.*, 1981; Breuer *et al.*, 1987) and propane-1,2,3-triol moiety due to two equivalent methylenes at  $\delta$  64.8 and a quaternary carbon at  $\delta$  75.5. These data led to identification of **1** as 5-hydroxy-6-acetyl-2-(2-propane-1,2,3-triol)-benzofuran, named gymnastone. This benzofuran structure was first isolated in nature.

Compound **2** was isolated as a yellow amorphous powder. In the <sup>1</sup>H-NMR spectrum, the acetyl group at  $\delta$  2.58 and two single peaks due to the phenyl protons at  $\delta$  6.83 and 7.08 were observed. The <sup>13</sup>C-NMR spectrum of **2** revealed the presences of the acetyl group at  $\delta$  27.1 and 203.9, six aromatic carbon signals at  $\delta$  108.4-158.5, a double bond-methylene group at  $\delta$  113.2. These data indicated **2** had similar *p*-hydroxyacetophenone structure.

Table I. NMR spectral data for compounds **1** and **2**

No	<b>1</b>		<b>2</b>	
	<sup>1</sup> H	<sup>13</sup> C	<sup>1</sup> H	<sup>13</sup> C
2	-	165.8	5.32 (1H, t, $J$ = 8.7)	83.9
3	6.75 (1H, s)	104.3	3.41 (1H, dd, $J$ = 8.7, 16.8 Hz) 3.18 (1H, dd, $J$ = 8.7, 16.8 Hz)	36.2
4	6.99 (1H, s)	107.1	6.83 (1H, s)	108.4
5	-	158.1	-	158.5
6	-	116.4	-	118.3
7	7.97 (1H, s)	112.6	7.08 (1H, s)	115.0
8	-	148.5	-	147.4
9	-	136.8	-	137.8
10	-	204.8	-	203.9
11	2.67 (3H, s)	25.9	2.58 (3H, s)	27.1
12	-	75.5	-	147.4
13	3.88 (4H, dd, $J$ = 11.1, 16.2 Hz)	64.8	5.27 (2H, s)	113.2
14	3.88 (4H, dd, $J$ = 11.1, 16.2 Hz)	64.8	4.27 (2H, d, $J$ = 13.2 Hz)	63.5

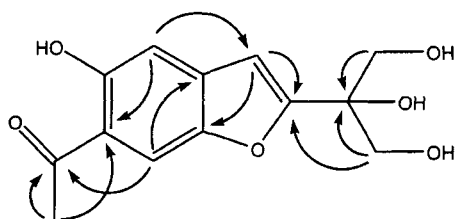


Fig. 2. HMBC correlation of **1**

By comparing physicochemical and spectral data with previously reported, compound **2** was identified to be viscidone which was isolated from *Chrysothamnus viscidiflorus* (Ngo and Pham, 1981) and *Baccharis truncata* (Bohlmann *et al.*, 1981).

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## REFERENCES

- Bohlmann, F., Kramp, W., Grenz, M., Robinson, H., and King, R. M., Diterpenes from *Baccharis* species. *Phytochemistry*, 20, 1907-1913 (1981).
- Breuer, M., Budzikiewicz, H., Siebertz, R., and Proksch, P., Benzofuran derivatives from *Ageratum houstonianum*. *Phytochemistry*, 26, 3055-3057 (1987).
- Jung, H. J., Min, B. S., Park, J. Y., Kim, Y. H., Lee, H. K., and Bae, K. H., Gymnasterkoreaynes A-F, cytotoxic polyacetylenes from *Gymnaster koraiensis*. *J. Nat. Prod.*, 65, 897-901 (2002).
- Ngo, L. V. and Pham, T. V. C., An unusual *m*-hydroxyacetophenone and three new chromanone derivatives from *Chrysothamnus viscidiflorus*. *Phytochemistry*, 20, 485-487 (1981).
- Park, J. Y., Min, B. S., Jung, H. J., Kim, Y. H., Lee, H. K., and Bae K. H., Polyacetylene glycosides from *Gymnaster koraiensis*. *Chem. Pharm. Bull.*, 50, 685-687 (2002).