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# A NEW SESQUITERPENE LACTONE FROM *Hosta ensata*

**Hong-xin Liu,[1,2] Qian-yun Sun,[3] Fu-mei Yang,[3] Fu-wei Zhao,[1,2] Yue-hu Wang,[1*] and Chun-lin Long[1,4*]**

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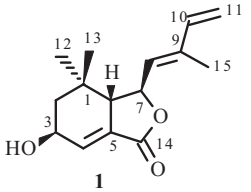
*A new monocyclofarnesane-type sesquiterpenoid, hostasolide A (**1**), along with five known compounds, lyciumide A, feruloyltyramine, dimethyl 4,4′-dihydroxy-3,3′-dimethoxy-β-truxinate, 4-hydroxy-3-methoxybenzaldehyde, and 3,4-dimethoxycinnamic acid, were isolated from the whole plant of* Hosta ensata. *The structure of compound **1** was determined on the basis of spectroscopic analysis. The inhibitory activities of compound **1** against acetylcholinesterase, human chronic myelogenous leukemia K562 cells, and human breast cancer MCF-7 cells were also evaluated.*

**Keywords**: Liliaceae, *Hosta ensata*, sesquiterpene, hostasolide A.

The genus *Hosta* (Liliaceae) comprises about 45 species. Most of them are distributed in temperate and subtropical Asia, especially in Japan. Only four species, *H. plantaginea*, *H. vertricosa*, *H. albofarinosa*, and *H. ensata*, occur in China, mainly in the Yangtze River basins. However, *H. ensata* F. Maekawa was also found in Jilin and Liaoning Provinces, northeast China [1]. The whole plant is used to treat diuresis, dysmenorrhea, ulcers, and carbuncles as a folk medicine in China [2]. *Hosta* plants contain mainly steroids and their glycosides [3–5] and flavonoid glycosides [6]. Also, a series of benzylphenethylamine alkaloids was found from *H. plantaginea* with inhibitory activity against tobacco mosaic virus (TMV) and acetylcholinesterase (AChE) [7]. Nevertheless, the chemical constituents of *H. ensata* are not clear yet. We conducted a phytochemical research on the whole plant of *H. ensata* and isolated a new sesquiterpene lactone hostasolide A (**1**) and five known compounds, lyciumide A [8], feruloyltyramine [9], dimethyl 4,4′-dihydroxy-3,3′-dimethoxy-*β*-truxinate [10, 11], 4-hydroxy-3-methoxybenzaldehyde [12], and 3,4-dimethoxycinnamic acid [13].

Hostasolide A (**1**) was obtained as an amorphous solid. The IR spectrum indicated the presence of hydroxy (3429 $cm^{-1}$) and ester carbonyl (1762 $cm^{-1}$) groups. Its molecular formula, $C_{15}H_{20}O_3$, was established on the basis of high-resolution ESI-MS for the $[M + Cl]^-$ ion at *m/z* 283.1106 (calcd 283.1101), indicating six degrees of unsaturation.

The NMR data of compound **1** (Table 1) exhibited signals for two trisubstituted double bonds [$\delta_H$ 6.74, 5.54; $\delta_C$ 134.7 (CH, C-4), 131.2 (C, C-5), 128.6 (CH, C-8), 140.2 (C, C-9)], one terminal double bond [$\delta_H$ 6.41, 5.34, 5.20; $\delta_C$ 139.9 (CH, C-10), 115.6 ($CH_2$, C-11)], an ester carbonyl [$\delta_C$ 169.1 (C, C-14)], two oxygenated methines [$\delta_H$ 4.48, 4.99; $\delta_C$ 66.6 (CH, C-3), 77.0 (CH, C-7)], three methyls, one $sp^3$ methylene, one $sp^3$ methine, and one $sp^3$ quaternary carbon group. Because four degrees of unsaturation are accounted for, the remaining two degrees of unsaturation must be due to two rings in **1**.

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1) Key Laboratory of Economic Plants and Biotechnology, Kunming Institute of Botany, Chinese Academy of Sciences, 650204, Kunming P. R. China, e-mail: wangyuehu@mail.kib.ac.cn; long@mail.kib.ac.cn; 2) Graduate University of Chinese Academy of Sciences, 100049, Beijing P. R. China; 3) Key Laboratory of Chemistry for Natural Products, Guizhou Province and Chinese Academy of Sciences, 550002, Guiyang P. R. China; 4) College of Life and Environmental Sciences, Minzu University of China, 100081, Beijing, P. R. China. Published in *Khimiya Prirodnykh Soedinenii*, No. 4, July–August, 2012, pp. 523–524. Original article submitted May 16, 2011.

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TABLE 1. $^1$H (400 MHz) and $^{13}$C NMR (100 MHz) Data of Compound **1** ($CDCl_3$, δ, ppm, J/Hz)

| Atom | $\delta_H$ | $\delta_C$ | Atom | $\delta_H$ | $\delta_C$ |
|---|---|---|---|---|---|
| 1 | | 35.3 C | 9 | | 140.2 C |
| 2$\alpha$ | 1.93 (1H, dd, J = 13.0, 4.5) | 47.0 $CH_2$ | 10 | 6.41(1H, dd, J = 17.4, 10.7) | 139.9 CH |
| 2$\beta$ | 1.45 (1H, dd, J = 13.0, 10.3) | | 11 | 5.34 (1H, d, J = 17.4) | 115.6 $CH_2$ |
| 3 | 4.48 (1H, m) | 66.6 CH | | 5.20 (1H, d, J = 10.7) | |
| 4 | 6.74 (1H, m) | 134.7 CH | 12 | 0.94 (3H, s) | 20.6 $CH_3$ |
| 5 | | 131.2 C | 13 | 1.01 (3H, s) | 29.2 $CH_3$ |
| 6 | 2.64 (1H, m) | 53.2 CH | 14 | 1.02 | 169.1 C |
| 7 | 4.99 (1H, t, J = 9.3) | 77.0 CH | 15 | 1.90 (3H, s) | 12.6 $CH_3$ |
| 8 | 5.54 (1H, d, J = 9.3) | 128.6 CH | | | |

The $^1$H–$^1$H COSY spectrum exhibited three partial structures, (C-2 to C-4), (C-6 to C-8), and (C-10 to C-11). Based on the HMBC correlations of $H_2$-2 to C-6, H-3 to C-5, H-4 to C-6 and C-14, $H_3$-12 and $H_3$-13 to C-2 and C-6, and $H_3$-15 to C-8 and C-10, a carbon skeleton of monocyclofarnesane-type in the sesquiterpenoid **1** was deduced. The additional ring in **1** should be a 14,3- or 14,7-olide ring. Because the chemical shifts of H-7 and C-7 were in lower field than those of H-3 and C-3, 7-OH should be esterified to form the 14,7-olide ring.

ROESY correlations of H-3/Me-12 and H-7/Me-12 showed that these protons were cofacial, and were arbitrarily assigned as the $\alpha$-orientation, while 3-OH and Me-13 were $\beta$-oriented. The correlations of H-6/Me-13 and H-6/H-8 showed H-6 to be in the $\beta$-orientation. The *E*-configuration of the 8,9-double bond was determined by ROESY correlations of H-7/Me-15 and H-8/H-10. Therefore, the structure of hostasolide A was elucidated as shown in **1**.

The results of bioassay showed that **1** was inactive against acetylcholinesterase [14], human chronic myelogenous leukemia K562 cells [15], and human breast cancer MCF-7 cells [16].

## EXPERIMENTAL

**General Experimental Procedures**. UV spectra were measured on a Shimadzu double-beam 210A spectrometer. IR spectra were determined on a Bio-Rad FTS-135 infrared spectrophotometer with KBr disks. 1D and 2D NMR spectra were recorded on Bruker AM-400 spectrometers with TMS as internal standard. ESI-MS analysis was carried out on an API Qstar Pulsar 1 instrument. EI-MS was carried out on a Waters Autospec Premier P776 mass spectrometer. Silica gel G (80–100 and 300–400 mesh, Qingdao Makall Group Co., Ltd.), MCI gel CHP 20P (75–150 μm, Mitsubishi Chemical Corporation, Tokyo), C18 silica gel (40–75 μm, Fuji Silysia Chemical Ltd.), and Sephadex LH-20 (GE Healthcare Bio-Sciences AB) were used for column chromatography (CC), and silica gel GF254 (Qingdao), for preparative TLC as precoated plates. TLC spots were visualized under UV light and by dipping into 5% $H_2SO_4$ in alcohol followed by heating.

**Plant Material**. The whole plant of *H. ensata*, collected from Linjiang City of Jilin Province, China in June 2010 was identified by Dr. Guang Wan Hu, and a voucher specimen was deposited at the Key Laboratory of Economic Plants and Biotechnology, Kunming Institute of Botany.

**Extraction and Isolation**. The air-dried powder of the plant material (5 kg) was exhaustively extracted with $CH_3OH$ three times, and the extract (1.1 kg) was suspended in $H_2O$ and partitioned with petroleum and EtOAc. The EtOAc-soluble part (35 g) was subjected to column chromatography (silica gel, $CHCl_3$–$CH_3OH$, 1:0→1:1) to afford six fractions. Fraction 1 ($CHCl_3$–$CH_3OH$, 1:0) was purified by repeated column chromatography over silica gel and preparative TLC to provide 4-hydroxy-3-methoxybenzaldehyde (8 mg) and 3,4-dimethoxycinnamic acid (15 mg). Fraction 2 ($CHCl_3$–$CH_3OH$, 10:1) was subjected to reversed-phase column chromatography over $C_{18}$ silica gel eluting with a gradient of increasing MeOH in $H_2O$ (5–95%) and subsequently chromatographed on a Sephadex LH-20 column (MeOH) and repeated silica gel column chromatography to afford **1** (14 mg), lyciumide A (10 mg), feruloyltyramine (20 mg), and dimethyl 4,4′-dihydroxy-3,3′-dimethoxy-$\beta$-truxinate (2 mg).

**Hostasolide A (1)**. Colorless amorphous solid, $[\alpha]_D^{21.9}$ +12.0° (*c* 0.54, $CHCl_3$). UV ($CHCl_3$, $\lambda_{max}$, nm) (log ε): 241 (3.52). CD Δ ε (*c* 0.0125, MeOH) + 5.00 (242), 0 (229), – 6.60 (217). IR (KBr, $\nu_{max}$, $cm^{-1}$): 3429, 1762, 1262, 1098, 1022, 801. For $^1$H and $^{13}$C NMR data, see Table 1. ESI-MS $[M - H]^-$ *m/z* 247, $[M + Cl]^-$ *m/z* 283; HR-ESI-MS $[M + Cl]^-$ *m/z* 283.1106 (calcd for $C_{15}H_{20}O_3Cl$, 283.1101).

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