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A NEW CHROMONE FROM *Ostericum koreanum*

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*A new chromone, methyl (*R*)-2-hydroxy-3-((*S*)-2-(2-hydroxypropan-2-yl)-4-methoxy-5-oxo-2,3-dihydro-5*H*-furo[3,2-g]chromen-7-yl)propanoate (named as osterichromone A (**4**)), along with known compounds hamaudol (**1**), angeliticin A (**2**), scopoletin (**3**), and cimifugin (**5**) were isolated from the stems of* Ostericum koreanum. *Their structures were elucidated using spectroscopic methods, including extensive 1D and 2D NMR techniques.*

Keywords: *Ostericum koreanum*, stems, chromones.

Ostericum koreanum (Maxim.) Kitag., a member of the Apiaceae family, is an important herbaceous plant in Korea. The roots of this plant have been used to treat common colds in traditional medicine [1]. Several coumarins, chromones, phenolic compounds, and quinic acid derivatives have been isolated from the roots of this plant. Their structures were reported in detail [2–5].

Recently, as part of our ongoing systematic phytochemical studies on Apiaceae in Korea, we isolated three coumarins, one chromone, and phytosterol mixtures from the nonpolar soluble fraction of the stem extract of *O. koreanum* [6].

In this study, we focused on the polar solvent soluble fraction of the stem extract of *O. koreanum* to isolate and identify the chemical constituents of this fraction. This led to the isolation of a new chromone along with four previously known compounds. Herein, we describe the isolation and structure elucidation of these compounds.

The isolated compounds were numbered from **1** to **5**. Compounds **1**, **2**, **3**, and **5** were identified as hamaudol [7], angeliticin A [8], scopoletin [9], and cimifugin [7], respectively, by comparing their spectral data with those reported in the literature.

The HR-EI-MS spectrum of compound **4** showed a molecular ion peak at *m/z* 378.1314, which is consistent with the formula $C_{19}H_{22}O_8$ (calcd 378.1315). The ^{1}H NMR spectrum of **4** exhibited two singlets at δ 6.60 (1H, H-9) and 6.26 (1H, H-6), a triplet at δ 4.74 (1H, t, J = 8.8 Hz), a doublet of doublets at δ 3.32 (1H, J = 15.9, 8.8 Hz), an overlapped multiplet at δ 3.30, two *gem*-$(CH_3)_2$ signals at δ 1.28 and 1.23, and a methoxy signal at δ 3.92. These signals were very similar to that of cimifugin, except for the signals of the functional group attached at the C-7 position [8]. Furthermore, the ^{1}H NMR signals exhibited a doublet of doublets at δ 4.90 (1H, J = 8.8, 4.3 Hz), a doublet of triplets at δ 2.92 (1H, J = 4.3, 15.5 Hz), a doublet of doublet of doublets at δ 2.72 (1H, J = 15.5, 8.8, 1.6 Hz), and a methyl ester singlet at δ 3.70. In addition, the ^{13}C NMR and 135° DEPT spectra exhibited a carbonyl signal at δ 171.02, an oxygen-bearing methine signal at δ 66.69, a methylene signal at δ 39.48, and a methyl ester signal at δ 51.00. This suggested that compound **4** had a methyl propanoate substituent. In the HMBC spectrum (Fig. 1), the methylene signals at δ_H 2.92 and 2.72 correlated with δ_C 171.02 (C-1″), 167.84 (C-7), and 66.69 (C-2″). This indicated that the methyl propanoate group was located at the C-7 position. The absolute configuration of compound **4** was further elucidated via ECD calculations. The calculated ECD curve for the (2*S*,2″*R*)-isomer was consistent with the experimental ECD spectrum (Fig. 2), thus confirming that compound **4** had a (2*S*,2″*R*) absolute configuration.

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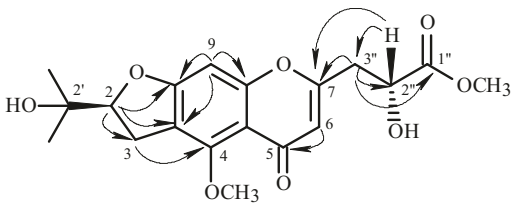

4

Fig. 1. Structure and key HMBC correlations for compound **4**.

Based on these results, it was deduced that the structure of compound **4** was methyl (*R*)-2-hydroxy-3-((*S*)-2-(2-hydroxypropan-2-yl)-4-methoxy-5-oxo-2,3-dihydro-5*H*-furo[3,2-g]chromen-7-yl)propanoate, further named as osterichromone A (Fig. 1).

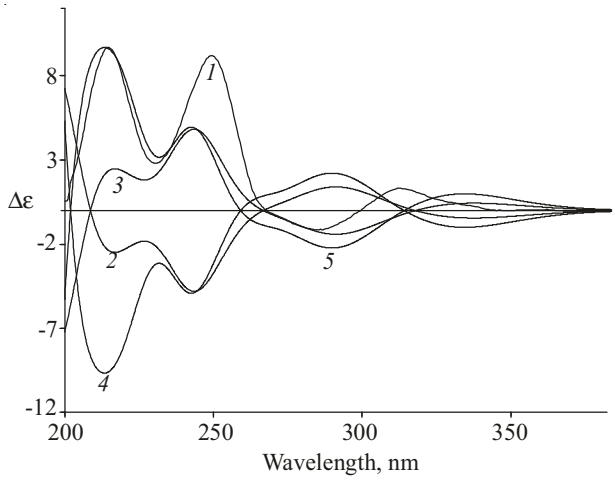

Fig. 2. Calculated and experimental ECD spectra of compound **4**. *1* – exptl.; *2* – calcd 2*R*2′′*R*; *3* - calcd 2*S*2′′*S*; *4* - calcd 2*R*2′′*S*; *5* - calcd 2*S*2′′*R*.

EXPERIMENTAL

General Experimental Procedures. ESI-MS spectra were measured using an API 3200 LC/MS/MS system (AB Sciex, Concord, Canada). The HR-EI-MS spectrum was measured using a JMS-700 spectrometer (JEOL, Tokyo, Japan). NMR spectra were recorded using a Bruker Avance 600 spectrometer (Bruker, Rheinstetten, Germany) and a JNM-ECZ400S/L1 spectrometer (JEOL, Tokyo, Japan). Optical rotation was performed on a DIP-1000 digital polarimeter (JASCO, Tokyo, Japan) and CD spectra were recorded on a Chirascan electronic circular dichroism (ECD) spectrometer (Applied Photophysics, Leatherhead, UK). Column chromatography was performed using a Kieselgel 60 (63–200 μm and 40–63 μm, Merck, Darmstadt, Germany) and YMC gel ODS-A (150 μm, YMC, Kyoto, Japan). Flash column chromatography was performed using the CombiFlash®, Retrieve™ system (Teledyne Isco Inc., NE, USA). Medium pressure liquid chromatography was performed using a Buchi 682 chromatography pump system (Buchi, Flawil, Switzerland). TLC was performed on glass-backed Kieselgel 60 F_{254} and RP F_{254s} plates. Distilled extra pure grade solvents (OCI Company Ltd., Incheon, Korea) were used for column chromatography analyses. All other chemicals and reagents used were of analytical grade.

Plant Material. The stems of *Ostericum koreanum* were collected from Mount Taegi, Pyeong Chang, Ganwondo Province, Korea, in August, 2016. A voucher specimen (KNUH-S-1608-1) was deposited at the Herbarium of the College of Pharmacy at Kangwon National University, Korea.

Extraction and Isolation. Air-dried *O. koreanum* stems (1.8 kg) were cut into small pieces and extracted three times with 80°C MeOH (10 L) under reflux conditions for 4 h. All extracts were filtered and concentrated *in vacuo* at 40°C. The MeOH extracts (116 g) were suspended in water and successively partitioned with *n*-hexane, EtOAc, and *n*-BuOH, leaving a residual water-soluble fraction. The obtained *n*-hexane, EtOAc, and *n*-BuOH soluble fractions were evaporated *in vacuo* to

yield the residues of the *n*-hexane (12 g), EtOAc (7 g), and *n*-BuOH extracts (13 g). The combined EtOAc and *n*-BuOH fractions (19 g) subjected to silica gel column chromatography (CC) (63–200 μm, 500 g, 11 × 50 cm) with isocratic elution using $CHCl_3$–MeOH (9:1) to obtain five fractions (OS-1–OS-5). Fraction OS-1 (3.1 g) was re-chromatographed using silica gel CC (63–200 μm, 3 × 50 cm, 200 g) with isocratic elution using benzene–EtOAc (4:1) to obtain six fractions (OS-1-1–OS-1-6). Fraction OS-1-3 (1.2 g) was further purified by ODS CC (150 μm, 70 g, 2 × 45 cm) with isocratic elution using MeOH–H_2O (70:30) to obtain compounds **1** (30 mg) and **2** (170 mg). Fraction OS-1-4 (0.6 g) was purified by ODS CC (150 μm, 70 g, 2 × 45 cm) with isocratic elution using MeOH–H_2O (50:50) to obtain compound **3** (50 mg). Fraction OS-2 (2.1 g) was re-chromatographed using silica gel CC (63–200 μm, 3 × 50 cm, 200 g) with isocratic elution using $CHCl_3$–MeOH (24:1) to obtain five fractions (OS-2-1–OS-2-5). Fraction OS-2-2 (0.4 g) was further purified using flash chromatography with Redi Sep silica gel (40 g, benzene–EtOAc, 4:1) to obtain compound **4** (10 mg). Fraction OS-3 (2.4 g) was further chromatographed over silica gel CC (63–200 μm, 4 × 50 cm, 200 g) with isocratic elution using $CHCl_3$–MeOH (9:1) to afford four subfractions (OS-3-1–OS-3-4). Subfraction OS-3-2 (1.8 g) was further purified by silica gel CC (40–63 μm, 3 × 50 cm, 100 g) with isocratic elution using *n*-hexane–EtOAc (1:14) to obtain compound **5** (596 mg).

Osterichromone A (4), white powder, $[\alpha]_D^{20}$ +25.9° (*c* 0.14, MeOH). ^{1}H NMR (600 MHz, CD_3OD, δ, ppm, J/Hz): 6.60 (1H, s, H-9), 6.26 (1H, s, H-6), 4.90 (1H, dd, J = 8.8, 4.3, H-2″), 4.74 (1H, t, J = 8.8, H-2), 3.92 (3H, s, OCH_3), 3.70 (3H, s, OCH_3), 3.32 (1H, dd, J = 15.9, 8.8, Ha-3), 3.30 (overlapped, m, Hb-3), 2.92 (1H, dt, J = 4.3, 15.5, Ha-3″), 2.72 (1H, ddd, J = 15.5, 8.8, 1.6, Hb-3″), 1.28, 1.23 (each 3H, s, gem-$(CH_3)_2$). ^{13}C NMR (150 MHz, CD_3OD, δ, ppm): 178.30 (C-5), 171.02 (C-1″), 167.84 (C-7), 165.77 (C-9a), 159.64 (C-8a), 155.62 (C-4), 117.14 (C-3a), 110.88 (C-4a), 107.99 (C-6), 93.14 (C-9), 91.52 (C-2), 70.83 (C-2′), 66.69 (C-2″), 59.64 (OCH_3), 51.00 (OCH_3), 39.48 (C-3″), 27.34 (C-3), 24.02 (C-1′), 23.93 (C-3′). EI-MS (*m/z*, $I_{rel.}$, %): 378 (M^+, 27.3), 360 (100), 342 (24.7), 327 (27.9), 313 (16.6), 301 (86.3), 283 (74.9), 271 (24.0), 259 (21.8), 241 (16.9), 227 (13.9), 217 (13.6), 201 (10.2), 59 (73.6); HR-EI-MS *m/z* 378.1314 (calcd for $C_{19}H_{22}O_8$, 378.1315).

ECD Analysis Procedures [10]. The Conflex 7 (Conflex Corp., Tokyo, Japan) software was used to conduct a conformational search of compound **4**. An initial geometry optimization was performed, followed by a conformational search using MMFF94s molecular force-field calculations (search limit of energy: 3.0 kcal/mol) to obtain the energy and population of each conformer. The major conformers of compound **4,** accounting for more than 80% of the total population, were selected and subjected to further optimization at the B3LYP/def-SV(P) level of theory in the gas phase using the TmoleX 4.4 and Turbomole (COSMOLogic GmbH, Leverkusen, Germany) software, followed by ECD calculations using time-dependent density functional theory at the B3LYP/def-SV(P) level in the gas phase. The resultant calculated curves of each conformer were weighed by the Boltzmann distribution of each conformer and the averaged spectra were generated using the SpecDis 1.70.1 (half-bandwidth of 0.30 eV) software derived from their relative free energy values, with an UV correction.

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REFERENCES

1. K. Bae, *Illustrations of natural medicines* [in Korean], Kyohaksa, Seoul, 2019, p. 886.
2. C. K. Lee and W. S. Woo, *Kor. J. Pharmacogn*., **13**, 10 (1982).
3. Y. S. Kwon, K. K. In, and C. M. Kim, *Kor. J. Pharmacogn*., **31**, 284 (2000).
4. Y. S. Kwon, E. R. Woo, and C. M. Kim, *Kor. J. Pharmacogn*., **22**, 156 (1991).
5. Y. J. Park, H. J. Kim, S. J. Lee, H. Y. Choi, C. Jin, and Y. S. Lee, *Chem. Pharm. Bull.*, **55**, 1065 (2007).
6. J. H. Ko, J. H. Keum, J. W. Jung, H. K. Jhee, S. P. Hong, M. J. Kim, W. Chun, and Y. Kwon, *Kor. J. Pharmcogn*., **51**, 158 (2020).
7. H. Sasaki, H. Taguchi, T. Endo, and I. Yosioka, *Chem. Pharm. Bull*., **30**, 3555 (1982).
8. C. F. Mi, C. D. Wang, B. L. Qiao, H. L. Shi, and F. X. Li, *Acta Pharm. Sin.*, **30**, 910 (1995).
9. Y. S. Kwon, S. J. Shin, M. J. Kim, and C. M. Kim, *Arch. Pharm. Res.*, **25**, 53 (2002).
10. G. Pescitelli and T. Bruhn, *Chirality*, **28**, 466 (2016).