Three New Homoisoflavanone Glycosides from the Bulbs of Ornithogalum caudatum

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Phytochemical examination of *Ornithogalum caudatum* led to the isolation of three new homoisoflavanone glycosides. Their structures were elucidated, on the basis of the spectroscopic data and chemical evidence and by comparing them with those of known compounds, as (-)-7-O-methyleucomol 5-O- β -D-glucopyranoside (1), (-)-7-O-methyleucomol 5-O- β -neohesperidoside (3), respectively.

The genus *Ornithogalum*, with some 150 species, belongs to the subfamily Schilloideae in Liliaceae and has a distribution in the temperate climates of Europe, Asia, and Africa.¹ Some *Ornithogalum* plants are known to be poisonous plants, and several cardenolide glycosides were isolated and identified.² Recently, several cholestane glycosides with potent cytostatic activity on various tumor cells were isolated from *O. saundersiae* bulbs.^{1,3}

Ornithogalum caudatum Ait., an annual herb distributed in southern Africa and introduced to China many years ago, is known in Chinese folk medicine to have anticancer, antimicrobial, and antiinflammatory activities and used to treat hepatitis, parotitis, and some tumors in northern China. Previous phytochemical studies on the whole plant revealed the presence of physcion, baicalin, and steroidal saponins, but to the best of our knowledge, there have been no prior studies on its bulbs. Herein we report the isolation of three new homoisoflavanone glycosides (1–3) from the bulbs of O. caudatum.

- 1 $R_1 = R_2 = H$
- 2 $R_1 = H$ $R_2 = \alpha$ -L-rha
- 3 $R_1 = \alpha$ -L-rha $R_2 = H$

A 95% EtOH extract of air-dried bulbs of *O. caudatum* was evaporated in vacuo, suspended in H_2O , and sussessively partitioned with CH_2Cl_2 and n-BuOH. The n-BuOH fraction was subjected to column chromatography over silica gel, Sephadex LH-20, and ODS HPLC. Three new homoisoflavanone glycosides (1–3) were obtained.

Compound 1 appeared as white needles (MeOH) with $[\alpha]_D^{24}-18.8^\circ$ (c 0.10, MeOH), whose molecular formula, $C_{24}H_{28}O_{11}$, was inferred from HRFABMS ([M - H] $^-$ m/z 491.1550). ^{13}C NMR and DEPT spectra showed 22 resonance lines, indicating two methyl, three methylene, nine

methine, and eight quaternary carbons. The IR spectrum of 1 exhibited absorption bands at 3497, 3476 (hydroxy), 1659 (flavanone carbonyl), 1614, 1566, 1513, 1471 (aromatic ring), and a broad band at 1170-1000 cm⁻¹, indicating its glycosidic nature. The ¹H, ¹³C NMR and DEPT data also indicated a glycoside structure for 1. The signals at δ 4.88 (1H, d, J = 7.2 Hz) and 101.7 (CH), respectively, were assignable to the anomeric proton and carbon of a glycosyl moiety, and a β -configuration at the anomeric carbon was suggested.⁵ Signals at δ_H 3.15–3.75 (6H, m) and δ_C 77.4, 76.1, 73.3, 69.8, and 60.7 were in good agreement with those of the glucopyranosyl moiety.6 The presence of a glucopyranosyl unit was confirmed by enzyme hydrolysis of 1 followed by the identification of glucose by TLC comparison with an authentic sample. In addition to the signals for the glycosyl moiety, the ¹H NMR spectrum revealed signals for two methoxyl groups at δ 3.81 and 3.73 (each 3H, s), one methylene [δ 3.92 (1H, d, J = 7.2 Hz) and δ 3.96 (1H, d, J = 7.2 Hz)] linked to an oxygen atom, one benzylic methylene [δ 2.78 (2H, brs)], and six aromatic protons. Furthermore, the ¹³C NMR and DEPT spectra showed 18 carbon signals due to four aromatic carbons (δ 165.5, 163.5, 160.1, and 158.0), each bearing an oxygen function, four aromatic carbons (δ 95.5, 97.4, 113.3, and 131.5), each carrying a proton, one aromatic carbon (δ 104.1) linked to a carbonyl, one alkyl-substituted aromatic carbon (δ 127.2), one flavanone carbonyl carbon (δ 192.3), one methylene carbon (δ 71.1) having an oxygen function, one benzylic methylene carbon (δ 38.5), two methoxyl carbons (δ 55.8, 59.9), and one quaternary carbon (δ 72.0) having an oxygen function. These spectral data suggested an eucoumol-type aglycon^{7,8} for 1 with two methoxyl groups. In the aromatic region of the ¹H NMR spectrum, H-3',5' and H-2',6' protons at δ 6.85 (2H, d, J = 8.7 Hz) and δ 7.14 (2H, d, J = 8.7 Hz), respectively, suggested a para-substituted B-ring. In addition, a 5,7-disubstituted A-ring was evident from two *meta*-coupling protons at δ 6.51 (1H, d, J = 2.3 Hz) and δ 6.29 (1H, d, J = 2.3 Hz) for H-6 and H-8, respectively. The positions for the two methoxyl groups were determined by correlations from the methoxyl protons at δ 3.81 to C-7 (δ 165.5) and from the another methoxyl protons at δ 3.73 to C-4′ (δ 158.0) in the HMBC spectrum. The long-range correlation between the anomeric proton (δ 4.88) and C-5 (δ 160.1) showed the glucopyranosyl moiety to be at C-5. The observation of NOE between H-G1 (δ 4.88) and H-6 (δ 6.51) in NOESY and NOEDS spectra supported this result. The positions of two

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methoxyl groups at C-7 and C-4' were also confirmed by the corresponding NOESY spectrum. Enzyme hydrolysis (almond emulsin) of a small amount of 1 afforded a substance, identified by optical rotation ($[\alpha]_D^{24} - 28^\circ$)⁷ and spectroscopic methods as (-)-7-O-methylecoumol, indicating that the absolute configuration of C-3 is $S(\alpha\text{-OH})$. All of these data demonstrated that compound **1** was (-)-7-O-methylecoumol 5-O- β -D-glucopyranoside.

The UV and IR spectra of 2 were very similar to those of 1. Its ¹H and ¹³C NMR spectra were also similar to those of 1, except that a disaccharide unit was suggested by the pair of anomeric proton resonances at δ 4.86 (1H, d, J = 7.3 Hz) and δ 4.36 (1H, brs) and anomeric carbon resonances at δ 101.6 and 101.0. Upon enzyme hydrolysis of **2**, (-)-7-O-methylecoumol was identified by optical rotation⁷ and spectroscopic methods.^{7,8} The molecular formula, $C_{30}H_{38}O_{15}$, was inferred from the HRFABMS ([M – H]⁻ m/z 637.2128), and it was also supported by ¹³C NMR and DEPT spectroscopy. The HMBC experiment showed a longrange correlation between C-5 (δ 160.1) and the anomeric proton (δ 4.86), revealing the site of glycosidation to be the 5-OH of (–)-7-*O*-methylecoumol. The observation of NOE between H" (δ 4.86) and H-6 (δ 6.50) in NOESY and NOEDS spectra supported this result. The ¹³C NMR chemical shifts of the carbohydrate moiety of 2 were comparable with literature values for the flavonoid rutinoside. 6,10 The site of glucose and rhamnose linkage was further supported by the glycosylation shift (ca. 6.4 ppm) of C-6" in glucose, also revealed by a long-range correlation between C-6" (δ 67.1) and the anomeric proton (δ 4.36) of rhamnose in the HMBC spectrum. The $J_{G1,G2}$ value of 7.3 Hz further indicated that the glucosyl moiety was connected to the aglycone by a β -linkage.⁵ The structure of compound 2 was therefore characterized as (-)-7-O-methylecoumol 5-O- β -rutinoside.

The molecular formula of compound 3 was confirmed as C₃₀H₃₈O₁₅ from the HRFABMS. NMR and other spectroscopic data were nearly identical with those of 2; the only difference was that the site of glucose and rhamnose linkage was rha1→glc2, suggested by the glycosylation shift (ca. 3.0 ppm) of C-2" in glucose, also revealed by a longrange correlation between C-2" (δ 76.3) and the anomeric proton (δ 5.12) of rhamnose in the HMBC spectrum. The ¹³C NMR chemical shifts of the carbohydrate moiety of 3 were very similar to literature values for the flavonoid neohesperidoside. 6,11 The $J_{\rm G1,G2}$ value of 7.4 Hz further indicated that the glucosyl moiety was connected to the aglycone by a β -linkage.⁵ Therefore, compound **3** was determined to be (-)-7-*O*-methylecoumol 5-*O*- β -neohes-

To date, only three ecoumol-type homoisoflavanones have been isolated from Eucomis bicolor Bak. (Liliaceae),7 Caesalpinia sappan L. (Leguminosae),8 and Scilla dracomontana Hilliard and Burtt (Hyacinthaceae). 12 Compounds 1-3 were the first reported glycosides having an ecoumol-type homoisoflavanone as the aglycone.

Compounds 1-3 were tested for in vitro antitumor activities against P388 (mouse leukemia) and A-549 (human pulmonary adenocarcinoma). No positive activities were observed.

Experimental Section

General Experimental Procedures. Melting points were determined on an Electrothermal 9200 micro melting point apparatus and are uncorrected. Optical rotations were recorded with a Perkin-Elmer model 241 polarimeter. UV and IR spectra were measured on a Shimadzu UV-1601 instrument and on a Perkin-Elmer 983 spectrometer, respectively. All

NMR spectra were run on a Bruker DRX-400 instrument operating at 400 MHz for ¹H and 100 MHz for ¹³C, using standard pulse sequences. Chemical shifts are reported on the δ scale in parts per million, downfield from TMS. Carbon multiplicities were determined from DEPT-135 and DEPT-90 experiments. All 2D NMR spectra were recorded using pulsed field gradients. ¹H-¹H correlations were observed in double quantum filtered (DQF) COSY and TOCSY experiments. Onebond ¹³C-¹H correlations were observed in a HMQC experiment. Long-range ¹³C-¹H correlations were observed in HMBC experiments. FABMS spectra were obtained on a JEOL JMS DX-303HF mass spectrometer. Column chromatography was performed on Si gel (Marine Chemical Factory, Qingdao, People's Republic of China), Sephadex LH-20 (Pharmacia), and RP-18 (Shimadzu). Other conditions were as previously described.13

Plant Material. The bulbs of O. caudatum Ait. were collected from Jilin Province, People's Republic of China, and the plant was identified by Dr. Tao Wu. After collection, the bulbs were allowed to dry at ambient temperature for about one week and were then crushed and immediately extracted. A voucher specimen (No. SIOC-Bio-1999102802) was deposited in the State Key Laboratory of Bio-organic and Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, People's Republic of

Extraction and Isolation. The dried and crushed bulbs of O. caudatum (7.8 kg) were extracted three times with 95% EtOH under reflux for 3 h each time, solvent was removed under reduced pressure, and the residue was dissolved in hot water. This residue was left in a refrigerator overnight and then filtered. The filtrate was partitioned with CH2Cl2 and n-BuOH, successively. The n-BuOH extract (352.2 g) was concentrated and subjected to Si gel column chromatography eluting with CHCl₃-MeOH (25:1) followed by MeOH to yield 13 fractions. Fraction 5 (28.6 g) was subjected to Si gel (CHCl3-MeOH, 10:1) and Sephadex LH-20 (MeOH) chromatography and was purified by HPLC (RP₁₈, 4 µm, 280 nm, MeOH–1% acetic acid, 25:75; **1**: $t_R = 18.75$ min; **2**: $t_R = 13.22$ min; **3**: $t_R = 12.45$ min) to give **1** (34 mg), **2** (26 mg), and **3** (20 mg), respectively.

(-)-7-O-Methylecoumol 5-O- β -D-glucopyranoside (1): white needles (MeOH), mp 198–199 °C; $[\alpha]_D^{24}$ –18.8° (c 0.01, MeOH); UV (MeOH) λ_{max} (log ϵ) 200 (4.25), 224 (4.45), 282 (3.86) nm; IR ν_{max}^{KBr} 3497, 3476, 1659, 1614, 1566, 1513, 1471, 1170~1000 cm⁻¹; ¹H NMR (DMSO- d_6 , 400 MHz) δ 7.14 (2H, d. J = 8.7 Hz, H-2',6'), 6.85 (2H, d. J = 8.7 Hz, H-3',5'), 6.51 (1H, d, J = 2.3 Hz, H-6), 6.29 (1H, d, J = 2.3 Hz, H-8), 4.88 (1H, d, J = 7.2 Hz, H-1"), 3.96 (1H, d, J = 7.2, H-2 α), 3.92 $(1H, d, J = 7.2, H-2\beta)$, 3.81 (3H, s, 7-OMe), 3.73 (3H, s, 4'-OMe), 3.72 (1H, m, H-6"), 3.45 (1H, m, H-6"), 3.38 (1H, m, H-5"), 3.33 (1H, m, H-2"), 3.31 (1H, m, H-3"), 3.16 (1H, m, H-4"), 2.78 (2H, brs, H-9); 13 C NMR (DMSO- d_6 , 100 MHz) δ 192.3 (C-4), 165.5 (C-7), 163.5 (C-8a), 160.1 (C-5), 158.0 (C-4'), 131.5 (C-2',6'), 127.2 (C-1'), 113.3 (C-3',5'), 104.1 (C-4a), 101.7 (C-1"), 97.4 (C-6), 95.5 (C-8), 77.4 (C-5"), 76.1 (C-3"), 73.3 (C-2"), 72.0 (C-3), 71.1 (C-2), 69.8 (C-4"), 60.7 (C-6"), 59.9 (4'-OMe), 55.8 (7-OMe), 38.5 (C-9); HRFABMS m/z 491.1550 $[M - H]^-$ (calcd for $C_{24}H_{27}O_{11}$, 491.1553).

(-)-7-*O*-Methylecoumol 5-*O*- β -rutinoside (2): white needles (MeOH), mp 207–208 °C; $[\alpha]_D^{24}$ –15.5° (c 0.01, MeOH); UV (MeOH) λ_{max} (log ϵ) 202 (4.14), 224 (4.42), 281 (3.90) nm; IR ν_{max}^{KBr} 3496, 3472, 1659, 1614, 1567, 1512, 1470, 1170–1000 cm⁻¹; ¹H NMR (DMSO- d_6 , 400 MHz) δ 7.14 (2H, d. J=8.8Hz, H-2',6'), 6.86 (2H, d. J = 8.8 Hz, H-3',5'), 6.50 (1H, d, J =2.2 Hz, H-6), 6.30 (1H, d, J = 2.2 Hz, H-8), 4.86 (1H, d, J =7.3 Hz, H-1"), 4.36 (1H, brs, H-1""), 3.96 (1H, d, J = 7.3 Hz, H-2 α), 3.92 (1H, d, J = 7.3 Hz, H-2 β), 3.80 (3H, s, 7-OMe), 3.73 (3H, s, 4'-OMe), 3.70-3.05 (m, other sugar protons), 2.78 (2H, brs, H-9), 0.98 (3H, d, J = 6.1 Hz, H-6""); ¹³C NMR (DMSO- d_6 , 100 MHz) δ 192.4 (C-4), 165.4 (C-7), 163.6 (C-8a), 160.1 (C-5), 157.9 (C-4'), 131.6 (C-2',6'), 127.2 (C-1'), 113.3 (C-3',5'), 104.1 (C-4a), 101.6 (C-1"), 101.0 (C-1""), 98.2 (C-6), 95.5

(C-8), 76.0 (C-5"), 76.5 (C-3"), 73.5 (C-2"), 72.0 (C-3 and C-4""), 71.2 (C-2), 70.8 (C-3"), 70.6 (C-2"), 70.0 (C-4"), 68.5 (C-5"), 67.1 (C-6"), 60.0 (4'-OMe), 55.8 (7-OMe), 38.5 (C-9), 18.0 (C-6"'); HRFABMS m/z 637.2128 [M - H]⁻ (calcd for $C_{30}H_{37}O_{15}$, 637.2132).

(-)-7-O-Methylecoumol 5-O- β -neohesperidoside (3): white needles (MeOH), mp 212–213 °C; $[\alpha]_D^{24}$ –17.2° (c 0.01, MeOH); UV (MeOH) λ_{max} (log ϵ) 201 (4.18), 225 (4.44), 281 (3.91) nm; IR ν_{max}^{KBr} 3491, 3478, 1659, 1614, 1567, 1512, 1470, 1170–1000 cm $^{-1}$; ¹H NMR (DMSO- d_6 , 400 MHz) δ 7.14 (2H, d. J = 8.8 Hz, H-2',6'), 6.88 (2H, d. J = 8.8 Hz, H-3',5'), 6.53 (1H, d, J = 2.4 Hz, H-6), 6.30 (1H, d, J = 2.4 Hz, H-8), 5.01(1H, d, J = 7.4 Hz, H-1''), 5.12 (1H, brs, H-1'''), 3.96 (1H, d, J)= 7.2 Hz, H-2 α), 3.92 (1H, d, J = 7.2 Hz, H-2 β), 3.82 (3H, s, 7-OMe), 3.75 (3H, s, 4'-OMe), 3.90-3.10 (m, other sugar protons), 2.78 (2H, brs, H-9), 1.19 (3H, d, J = 6.2 Hz, H-6"); ¹³C NMR (DMSO- d_6 , 100 MHz) δ 192.3 (C-4), 165.4 (C-7), 163.4 (C-8a), 160.0 (C-5), 157.9 (C-4'), 131.5 (C-2',6'), 127.2 (C-1'), 113.3 (C-3',5'), 104.1 (C-4a), 100.5 (C-1"), 100.4 (C-1""), 97.3 (C-6), 95.4 (C-8), 77.4 (C-3"), 76.8 (C-5"), 76.3 (C-2"), 71.9 (C-3 and C-4"), 71.2 (C-2), 70.4 (C-3"), 70.5 (C-2"), 69.8 (C-4"), 68.2 (C-5"), 60.6 (C-6"), 59.9 (4'-OMe), 55.7 (7-OMe), 38.5 (C-9), 18.1 (C-6"); HRFABMS m/z 637.2130 [M – H]⁻ (calcd for C₃₀H₃₇O₁₅, 637.2132).

Enzyme Hydrolysis of Compounds 1-3. A solution of each compound (1-3, 10 mg) in HOAc-NaOAc buffer solution (pH 5.0, 10 mL) was treated with β -glucosidase (almond emulsin, G4511, Sigma Co., 8 mg) and kept stirring at 38 °C for 3 days. After addition of a small amount of CHCl3 and warming for a while, the total mixture was filtered. The filtrate was extracted with CHCl₃, and the CHCl₃ extract was evaporated under reduced pressure to give the product, which was purified by preparative TLC (*n*-hexane–EtOAc, 5:1) to furnish (-)-7-O-methylecoumol, identified by optical rotation and spectroscopic methods.^{7,8}

Biological Tests. The in vitro antitumor activity assays were carried out following the methods of Nakamura et al. 14

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References and Notes

- (a) Kubo, S.; Mimaki, Y.; Sashida, Y.; Nikaido, T.; Ohmoto, T. Bull. Chem. Soc. Jpn. **1992**, 65, 1120–1124. (b) Kubo, S.; Mimaki, Y.; Terao, M.; Sashida, Y.; Nikaido, T.; Ohmoto, T. Phytochemistry 1992, 31, 3969-3973.
- (a) Ghannamy, U.; Kopp, B.; Robien, W.; Kubelka, W. Planta Med. 1987, 53, 172–178. (b) Ferth, R.; Baumann, A.; Robien, W.; Kopp, B. Z. Naturforsch., B: Chem. Sci. 1992, 47, 1448–1458. (c) Ferth, R.; Baumann, A.; Mayer, K. K.; Robien, W.; Kopp, B. Z. Naturforsch., B: Chem. Sci. 1992, 47, 1459-1468.
- (a) Kuroda, M.; Mimaki, Y.; Sashida, Y.; Nikaido, T.; Ohmoto, T. Tetrahedron Lett. **1993**, *34*, 6073–6076. (b) Kuroda, M.; Mimaki, Y.; Sashida, Y.; Hirano, T.; Oka, K.; Dobashi, A. Chem. Pharm. Bull. **1995**, *43*, 1257–1259. (c) Mimaki, Y.; Kuroda, M.; Sashida, Y.; Hirano, T.; Oka, K.; Dobashi, A. Tetrahedron Lett. **1996**, *37*, 1245–1248. (d) Mimaki, Y.; Kuroda, M.; Kameyama, A.; Sashida, Y.; Hirano, T.; Oka, Mimaki, Y.; Kuroda, M.; Kameyama, A.; Sashida, Y.; Hirano, T.; Oka, K.; Koike, K.; Dobashi, A. *Biosci. Biotech. Biochem.* **1996**, *60*, 1049–1050. (e) Hirano, T.; Oka, K.; Mimaki, Y.; Kuroda, M.; Sashida, Y. *Life Sci.* **1996**, *58*, 789–798. (f) Mimaki, Y.; Kuroda, M.; Kameyama, A.; Sashida, Y.; Hirano, T.; Oka, K. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 633–666. (g) Kuroda, M.; Mimaki, Y.; Sashida, Y.; Hirano, T.; Oka, K.; Dobashi, A. *Tetrahedron* **1997**, *53*, 11549–11562. (h) Kuroda, M.; Mimaki, Y.; Sashida, Y.; Parkeide, Y. Sashida, Y.; Parkeide, Y. Sashida, Y.; Sashida, Y.; Sashida, Y.; Sashida, M.; Mimaki, Y.; Sashida, Y.; Sashida, M.; Mimaki, Y.; Sashida, Y. *Phytochemistry* **1999**, *52*, 435–443. (i) Kuroda, M.; Mimaki, Y.; Sashida, Y. *Phytochemistry* **1999**, *52*, 445–
- 452. (j) Kuroda, M.; Mimaki, Y.; Yokosuka, A.; Sashida, Y.; Beutler, J. A. *J. Nat. Prod.* **2001**, *64*, 88–91. (a) Liu, D.; Wang, K.; Zhang, H.; Chen, W.; Chen, Z. *Zhongcaoyao* **1998**, *29*, 443–444. (b) Xu, T.; Xu, Y.; Liu, D.; Xu, D. *Yaoxue Xuebao* **2000**, 35, 32-36.
- Markham, K. R.; Geiger, H. In The Flavonoids: Advances in Research since 1986; Harborne, J. B., Ed.; Chapman & Hall: London, 1994; pp 441-497.
- (a) Markham, K. R.; Terlai, B.; Stanley, R.; Geiger, H.; Mabry, T. L. *Tetrahedron* **1978**, *34*, 1389–1397. (b) Tang, Y.; Wang, Y.; Lou, F.;
- Li, Y.; Wang, J. *Yaoxue Xuebao* **2000**, *35*, 363–366. (a) Böhler, P.; Tamm, C. *Tetrahedron* **1967**, (36) 3479–3483. (b) Heller, W.; Andermatt, P.; Schaad, W. A.; Tamm, C. *Helv. Chim. Acta* **1976**, 59, 2048-2058.
- Saitoh, T.; Sakashita, S.; Nakata, H.; Shimokawa, T.; Kinjo, J.; Yamahara, J.; Yamasaki, M.; Nohara, T. Chem. Pharm. Bull. 1986, *34*, 2506–2511
- (9) Weber, H. P.; Heller, W.; Tamm, C. Helv. Chim. Acta 1977, 60, 1388-1392.
- Tang, Y.; Wang, J.; Li, Y.; Lou, F.; Ma, W. Zhiwu Ziyuan Yu Huanjing
- Xuebao **2001**, 10, 59–60.
 (11) Freitag, P.; Mues, R.; Brill-Fess, C.; Stoll, M.; Zinsmeister, H. D.; Markham, K. R. *Phytochemistry* **1986**, *25*, 669–671.
- Crouch, N. R.; Bangani, V.; Mulholland, D. A. Phytochemistry 1999, 51, 943-946.
- Tang, Y.; Zheng, W.; Lou, F.; Li, Y.; Wang, J. J. Chin. Pharm. Sci. **2000**. *9*. 119–121.
- Nakamura, T.; Komori, C.; Lee, Y.; Hashimoto, F.; Yahara, S.; Nohara, T.; Ejima, A. Biol. Pharm. Bull. 1996, 19, 564-566.

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