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QIANHUCOUMARIN I FROM *PEUCEDANUM PRAERUPTORUM*

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Key Word Index—*Peucedanum praeruptorum*; Umbelliferae; qianhucoumarin I; angular dihydropyranocoumarins.

Abstract—A new angular dihydropyranocoumarin, named qianhucoumarin I was isolated from the root of *Peucedanum praeruptorum*. By spectral analysis and chemical evidence, the structure was elucidated as 3′(*S*)-acetoxy-4′(*S*)-tigloyloxy-3′,4′-dihydroseselin, and the absolute configurations were established by chemical correlation with known compounds.

INTRODUCTION

The roots of *Peucedanum praeruptorum* Dunn is known as a famous traditional Chinese medicine, Qianhu, which can be used to cure some diseases such as cough due to pathogenic wind-heat, accumulation of phlegm and heat in the lung. Some major compounds of angular dihydropyranocoumarins in the plant show calcium antagonistic activity [1]. The structural elucidation of several new coumaris [2–4] from the plant have been reported. In the present paper, the isolation and structural elucidation of another new coumarin, named qianhucoumarin I (**1**) are reported. By a combination of spectral analysis and chemical evidence, the structure of **1** was elucidated as 3′(*S*)-acetoxy-4′(*S*)-tigloyloxy-3′,4′-dihydroseselin, and the absolute configurations were established by chemical correlation with known compounds.

RESULTS AND DISCUSSION

Compound **1** was isolated as white cubic crystals. The molecular ion peak at *m/z* 386.1351 in the HR mass spectrum showed the molecular formula was $C_{21}H_{22}O_7$. The signals at 1718, 1642 and 1605 cm^{-1} in the IR spectrum were assigned to carbonyl and aromatic systems of a coumarin skeleton. The ^1H NMR spectrum in the aromatic proton region of **1** contained two pairs of doublets at δ 6.24 (1H, *d*, $J = 9.5$ Hz) and 7.61 (1H, *d*, $J = 9.5$ Hz) and 7.36 (1H, *d*, $J = 8.6$ Hz) and 6.82 (1H, *d*, $J = 8.6$ Hz), which are identical with the C-3-H and C-4-H signals of the α-pyrone ring system and signals of C-5-H and C-6-H of the benzene ring, indicating **1** was a kind of coumarin substituted at the C-7 and C-8 positions. A pair of doublets at δ 5.35 (1H, *d*, $J = 4.8$ Hz) and 6.59 (1H, *d*, $J = 4.8$ Hz) were assigned to the methine protons at C-3′-H and C-4′-H linked to two ester groups, showing that C-7 and C-8 of **1** formed a dihydropyran ring. The signals at δ 2.10 (3H, *s*) was due to an acetyl group and at δ 6.81 (1H, *m*), 1.74 (3H, *br d*) and 1.85 (3H, *br s*) were due to an tigloyl group.

On partial alkaline hydrolysis, **1** produced another coumarin which was identified as 3′(*S*)-acetoxy-4′(*S*)-hydroxy-3′,4′-dihydroseselin (**2**) by spectral analysis. On the basis of the evidence, it was considered that the acetoxy was attached to C-3′ and the tigloyloxy to C-4′.

There are two chiral carbon atoms in the molecular structure of **1**; it was reported that the relative configuration of the type of compounds can be determined by ^1H NMR. The relative configuration at C-3′ and C-4′ was considered to be *cis* on the basis of the coupling constant of C-3′-H and C-4′-H being 4.8 Hz and the difference in the methyl proton signals at δ 1.46 and 1.43 of the 2′-*gem*-dimethyl group being 0.03 ppm [5–7]. Compound **1** was a dextro-compound and its absolute configurations were studied further by chemical correlation with known compounds. On total alkaline hydrolysis, **1** gave a mixture of two products, isolated by HPLC. The compounds were identified by spectral analysis and optical activity as (−)-*cis*-khellactone (**3**) and (+)-*trans*-khellactone (**4**) as a minor artefact arising from epimerization at C-4′ because of the benzyl effect and SN_2 reaction mechanism (Scheme 1). The absolute configurations of **3** and **4** were described previously as 3′*S*, 4′*S* and 3′*S*, 4′*R* by chemical methods and X-ray diffraction analysis [8, 9] and, accordingly, the absolute configurations of **1** were

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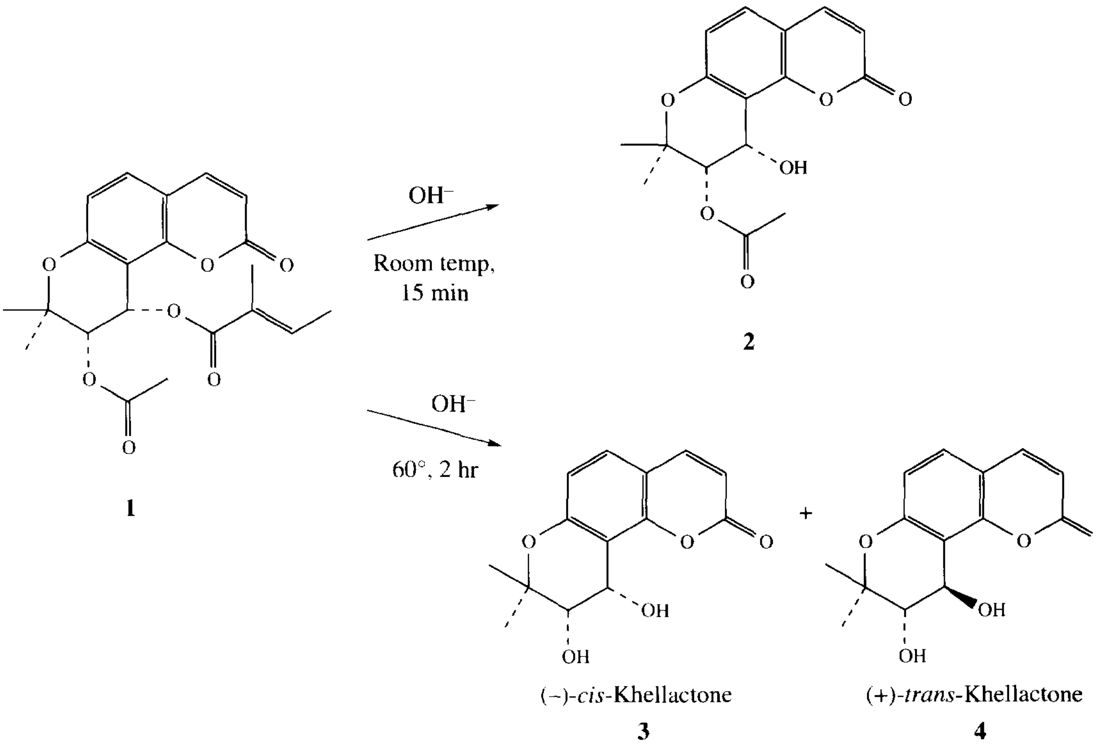

Scheme 1. Reactions of partial and total alkaline hydrolysis of **1**.

established as 3′S, 4′S. The chemical structure of **1** was finally elucidated as 3′(S)-acetoxy-4′(S)-tigloyloxy-3′,4′-dihydroseselin.

EXPERIMENTAL

MPS were determined on a Yanaco MP-S$_3$ micro melting-point apparatus, the thermometer was uncorr. UV spectra were recorded on a Shimadzu UV-260 spectrophotometer in MeOH soln. IR spectra were obtained on a Perkin-Elmer 983 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-AM-400 and a Bruker-AM-500 spectrometers using TMS as int. standard. EIMS were measured on a JEOL-DX-300 mass spectrometer. $[\alpha]_D$ values were determined on a Perkin-Elmer 241 automatic polarimeter at 20°.

Silica gel H (10–40 μm) was used for CC. Petrol refers to that fr. having bp 60–90°. Prep. HPLC was carried out on a Shimadzu Liquid Chromatograph LC-6A equipped with a UV detector, using a Shim-Pack PREP-SIL column (10 mm × 250 mm, Shimadzu), detector wavelength: 320 nm, flow rate: 4.0 ml min^{-1}, mobile phase: cyclohexane–EtOAc (4:1) for purification of the natural compound and cyclohexane–EtOAc (11:9) for sepn of the products of partial alkaline hydrolysis. CHCl$_3$–MeOH (49:1) was used for sepn for the products of total alkaline hydrolysis.

Plant material. Roots of *P. praeruptorum* Dunn were collected in Wuyi county, Zhejiang Province, China, in September, 1990 and identified by Prof. Chunquan Xu, Shenyang Pharmaceutical University, China, and deposited in the Research Department of Natural Medicines of this university.

Compound separation and structural elucidation. The root material was extracted with petrol, the concentrate was subjected to silica gel CC and eluted with petrol–EtOAc (22:3) to yield a fr. containing **1**. The fr. was further purified repeatedly by HPLC to yield **1** (36 mg).

Qianhucoumarin I (**1**). Cubic crystals, mp 142.5–144.0° (petrol-EtOAc). $[\alpha]_D^{20}$ +21.9° (c 0.15, CHCl$_3$). HRMS: M_r calc. 386.1366 for $C_{21}H_{22}O_7$, Obs. 386.1351. UV λ_{max}^{MeOH} nm: 244.8, 255.4, 321.9. IR ν_{max} cm^{-1}: 3035, 2976, 2930, 2852, 1745, 1718, 1642, 1605, 1572, 1400, 1371, 1345, 1232, 1144, 1068, 912, 894. ^{1}H NMR (400 MHz, CDCl$_3$): δ 6.24 (1H, *d*, J = 9.5 Hz, H-3), 7.61 (1H, *d*, J = 9.5 Hz, H-4), 7.36 (1H, *d*, J = 8.6 Hz, H-5), 6.82 (1H, *d*, J = 8.6 Hz, H-6), 5.35 (1H, *d*, J = 4.8 Hz, H-3′), 6.59 (1H, *d*, J = 4.8 Hz, H-4′), 1.46 (3H, *s*, C-2′-Me), 1.43 (3H, *s*, C-2′-Me), 2.10 (3H, *s*, H-2″), 6.81 (1H, *m*, H-3‴), 1.74 (3H, *br d*, J = 6.6 Hz, H-4‴), 1.85 (3H, *br s*, H-5‴). ^{13}C NMR (100 MHz, CDCl$_3$): δ 159.82 (C-2), 113.27 (C-3), 143.12 (C-4), 129.13 (C-5), 114.61 (C-6), 156.72 (C-7), 106.94 (C-8), 154.19 (C-9), 112.51 (C-10), 77.68 (C-2′), 69.73 (C-3′), 60.45 (C-4′), 25.49 (C-2′-Me), 22.75 (C-2′-Me), 169.38 (C-1″), 20.71 (C-2″), 166.29 (C-1‴), 138.02 (C-2‴), 128.34 (C-3‴), 12.33 (C-4‴), 14.48 (C-5‴). EIMS *m/z*: 386 $[M]^+$, 326 $[M\text{-}HOAc]^+$, 311, 287 $[M\text{-tigloyloxy}]^+$, 245, 229, 213, 83 (100), 55, 43.

Partial alkaline hydrolysis of **1**. A soln of **1** (12 mg) in dioxane (1 ml) containing 0.5 N KOH (0.5 ml) was stirred at room temp for 15 min. The reaction mixt. was acidified with 10% H_2SO_4, extracted with $CHCl_3$, and evapd to yield a major product, which was subjected to HPLC. The resulting compound needles, 5 mg, was **2**. Mp 155.0–156.5° (petrol–EtOAc), $[\alpha]_D^{20}$ +18.5° (*c* 0.05, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.25 (1H, *d*, $J = 9.5$ Hz, H-3), 7.64 (1H, *d*, $J = 9.5$ Hz, H-4), 7.33 (1H, *d*, $J = 8.6$ Hz, H-5), 6.79 (1H, *d*, $J = 8.6$ Hz, H-6), 5.42 (1H, *d*, $J = 4.9$ Hz, H-3′), 5.18 (1H, *d*, $J = 4.9$ Hz, H-4′), 1.48 (3H, *s*, C-2′-Me), 1.40 (3H, *s*, C-2′-Me), 1.25 (1H, *s*, OH), 2.18 (3H, *s*, H-2″). ^{13}C NMR (125 MHz, $CDCl_3$): δ 160.31 (C-2), 112.66 (C-3), 143.78 (C-4), 128.70 (C-5), 114.61 (C-6), 156.05 (C-7), 110.76 (C-8), 154.50 (C-9), 112.42 (C-10), 77.66 (C-2′), 72.52 (C-3′), 60.20 (C-4′), 25.38 (C-2′-Me), 22.63 (C-2′-Me), 170.28 (C-1″), 20.74 (C-2″). EIMS *m/z*: 304 $[M]^+$, 244, 191, 167, 149 (100), 119, 117, 55, 43.

Total alkaline hydrolysis of **1**. Compound **1** (20 mg) dissolved in dioxane (2.0 ml) with 0.5 N KOH (4.0 ml) and the soln was stirred at 60° for 2 hr. The soln was neutralized with 10% H_2SO_4, extracted with $CHCl_3$, washed with 10% $NaHCO_3$, dried with Na_2SO_4 and evapd. The residue was subjected to HPLC to separate two pure products. The first eluate (6 mg) gave **3**, needles, mp 170.0–171.5° (cyclohexane–EtOAc), $[\alpha]_D^{20}$ −72.8° (*c* 0.05, $CHCl_3$). ^{1}H NMR (500 MHz, CD_3OD): δ 6.24 (1H, *d*, $J = 9.5$ Hz, H-3), 7.86 (1H, *d*, $J = 9.5$ Hz, H-4), 7.46 (1H, *d*, $J = 8.6$ Hz, H-5), 6.78 (1H, *d*, $J = 8.6$ Hz, H-6), 3.77 (1H, *d*, $J = 4.9$ Hz, H-3′), 5.11 (1H, *d*, $J = 4.9$ Hz, H-4′), 1.43 (3H, *s*, C-2′-Me), 1.42 (3H, *s*, C-2′-Me), 3.35 (1H, *s*, OH), 2.16 (1H, *s*, OH). EIMS *m/z*: 262 $[M]^+$, 191 (100), 162, 134, 72. The second eluate (4 mg), which contained the artefact of epimerization at C-4′, gave **4**, needles, mp 182.5–184.0° (cyclohexane–EtOAc), $[\alpha]_D^{20}$ +19.4° (*c* 0.05, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.24 (1H, *d*, $J = 9.5$ Hz, H-3), 7.64 (1H, *d*, $J = 9.5$ Hz, H-4), 7.30 (1H, *d*, $J = 8.6$ Hz, H-5), 6.78 (1H, *d*, $J = 8.6$ Hz, H-6), 3.85 (1H, *d*, $J = 6.7$ Hz, H-3′), 4.99 (1H, *d*, $J = 6.7$ Hz, H-4′), 1.52 (3H, *s*, C-2′-Me), 1.31 (3H, *s*, C-2′-Me), 1.26 (2H, *s*, 2 OH). EIMS *m/z*: 262 $[M]^+$, 191 (100), 162, 134, 72.

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