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2-ISOPROPYL-6-METHYLPYRIMIDIN-4(3*H*)-ONE AND TARAXASTEROL FROM THE STEMS OF *Cichorium glandulosum*

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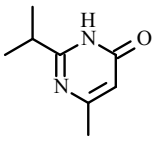
Cichorium glandulosum Boiss. et Huet. (Asteraceae) is well known in Uyghur folk medicine as a cholagogic and diuretic agent to improve the appetite, to increase digestion, and to cure liver diseases, etc. [1]. This plant is widely distributed in Xinjiang, but its chemical composition has not been studied thoroughly. Previously, the author reported the phytochemical study of the plant [2–5]. The pharmacological property of the traditional Uyghur medicinal plant *C. glandulosum* has attracted our research interests in recent years [6]. We have found the hepatoprotective activity of *C. glandulosum* extracts [7]. In order to clarify the chemical basis of the herb, which is often used to treat metabolic disorders such as diabetes and dyspepsia, the stems of *C. glandulosum* were selected for further study. To our great surprise, we found an *N*-containing compound, which was 2-isopropyl-6-methylpyrimidin-4(3*H*)-one (**1**), and its chemical structure was determined by X-ray single-crystal diffraction (Fig. 1) and NMR analysis. In addition, 21α-hydroxy-taraxasterol (**2**) was isolated and elucidated by NMR as well as by comparison with literature data. The above compounds were found in the stems of *C. glandulosum* for the first time.

Reagents and Equipments. All solvents were of analytical grade. NMR spectra were recorded on a Varian Unity Inova instrument (400 and 600 MHz), with chemical shifts in ppm relative to the solvent used. Column chromatography (CC) was performed using silica gel, and HSGF254 plates for thin layer chromatography (TLC) were products of Yantai Zhifu Huangwu Silica Gel Factory (Yantai, China). Gel filtration chromatography was performed on Sephadex LH-20 (25–100 mm, Fluka).

Plant Material. The stems of *Cichorium glandulosum* were purchased from Jimsar County, Xinjiang Uyghur Autonomous Reign, People′s Republic of China in October, 2007 and were identified by Prof. Shi-Ming Duan of the Xinjiang Institute of Ecology and Geography, Chinese Academy of Sciences. A voucher specimen was deposited at the Xinjiang Institute of Physics and Chemistry, Chinese Academy of Sciences, P. R. China.

Extraction and Isolation. The air-dried stems of *C. glandulosum* (6 kg) were cut into pieces and extracted at room temperature with 95% ethanol. The extract was concentrated under reduced pressure to give 720 g of crude residue. The residue was partitioned between water and chloroform. The chloroform layer afforded 280 g residue, which was further partitioned between petroleum ether and 90% MeOH (aqueous); 228 g (CGA4) of extract was obtained from 90% methanol layer after evaporation; 200 g of CGA4 was first fractionated by CC (2 kg of silica gel, PE–AcOEt 50:1, 30:1, 15:1, 10:1, 7:1, 5:1, 3:1, 1:1, 1:3) to give eight main fractions: Fr. A–I. Compound **1** (1.3 g) was crystallized from Fr. F (petroleum ether–AcOE 5:1), and compound **2** (20 mg) was obtained after separation on Sephadex LH-20 ($CHCl_3$–MeOH 1:1) and CC (PE–AcOE 15:1, 10:1 and 8:1) from Fr. C.



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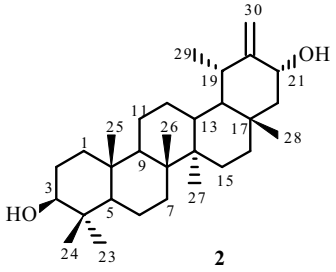

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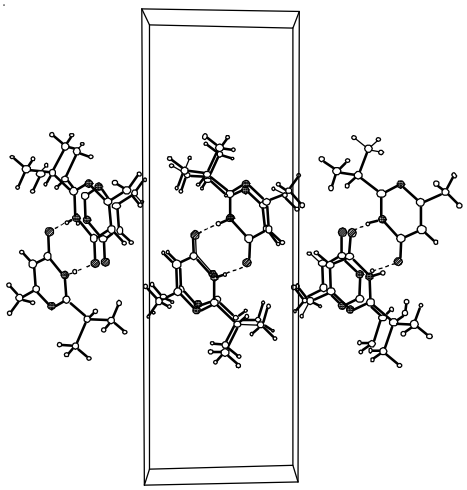

Fig. 1. Structure of 2-isopropyl-6-methylpyrimidin-4(3*H*)-one (**1**).

Compound 1. 2-Isopropyl-6-methylpyrimidin-4(3*H*)-one, colorless crystals, mp 172–174°C. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm, J/Hz): 13.1 (1H, s, NH), 6.16 (1H, d, J = 0.8, H-6), 2.92 (1H, heptet, J = 6.8, H-3), 2.29 (3H, d, J = 0.8, 8-CH_3), 1.32 (6H, d, J = 6.8, 1-CH_3 and 2-CH_3). ^{13}C NMR (100 MHz, DMSO, δ): 166.6 (C-5), 166.1 (C-7), 165.6 (C-4), 110.1 (C-6), 34.5 (C-3), 24.2 (C-8), 20.5 (C-1), 20.5 (C-2).

Crystallographic Data of 1. $C_8H_{12}N_2O$; Mr 152.20; crystal size: 0.80 × 0.71 × 0.62 mm; crystal system: monoclinic; space group P2 (1)/n; unit-cell dimensions: a = 4.8823 (10), b = 22.637 (5), c = 7.4487 (15) Å, α = 90.00, β = 96.57 (3), γ = 90.00°, V = 817.8 (3)Å ^{3}; Z = 4; Dx = 1.236 mg/m^3; F(000) = 328, T = 153 (2) K. Diffraction data of **1** were collected with a Rigaku R-Axis Spider area-detector diffractometer, using graphite-monochromated MoK_α radiation (λ = 0.71073 Å) and the ω to 2θ scan mode. The total number of reflections measured was 7820, of which 1868 were observed. Final indices: R_f 0.0389, R_w 0.0983. The structure was solved by direct methods using SHELXS-97 and refined by full-matrix least-squares on F^2 using SHELXL-97.

Compound 2. 21α-Hydroxy-taraxasterol, white powder, mp 246–248°C. ^{1}H NMR (600 MHz, $CDCl_3$, δ, ppm, J/Hz): 0.69 (1H, d, J = 10.2, H-5), 0.76 (3H, s, H-23), 0.76 (3H, s, H-28), 0.85 (3H, s, H-25), 0.93 (3H, s, H-27), 0.95 (3H, s, H-26), 1.02 (3H, s, H-24), 1.21 (3H, d, J = 7.2, H-29), 1.32 (1H, m, H-22), 1.95 (1H, dd, J = 13.2, 9 Hz, H-22), 2.15 (1H, quin, J = 7.2, H-19), 3.21(1H, dd, J = 11.4, 4.2, H-3), 4.39 (1H, dd, J = 8.4, 5.4, H-21), 4.98 (1H, br.s, H-30a), 4.89 (1H, br.s, H-30b). ^{13}C NMR (125 MHz, DMSO-d_6, δ): 38.7 (C-1), 27.4 (C-2), 78.9 (C-3), 38.9 (C-4), 55.3 (C-5), 18.3 (C-6), 34.0 (C-7), 40.9 (C-8), 50.4 (C-9), 37.1 (C-10), 21.4 (C-11), 26.2 (C-12), 38.9 (C-13), 42.2 (C-14), 26.4 (C-15), 37.7 (C-16), 33.9 (C-17), 48.4 (C-18), 38.1 (C-19), 156.6 (C-20), 71.3 (C-21), 48.8 (C-22), 27.9 (C-23), 15.4 (C-24), 16.3 (C-25), 15.9 (C-26), 14.8 (C-27), 18.2 (C-28), 28.4 (C-29), 113.6 (C-30). These data agreed with those in the literature [8–10]. However, in the process of structural elucidation, compound **2** was found to be not cichoridiol (a triterpene discovered from *Cichorium intybus* by Atta-ur-Rahman) [11]. The difference is that the C-19 methyl group of compound **2** was α-oriented and that of cichoridiol was β-oriented.

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