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Taraxacin, a New Guaianolide from *Taraxacum wallichii*

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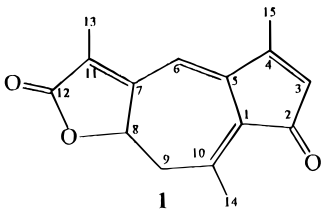
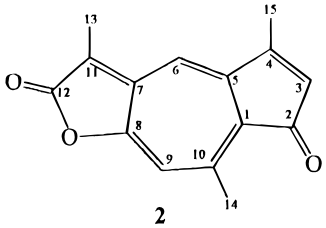
A new guaianolide, taraxacin (**1**), and a known sesquiterpene ketolactone (**2**) have been isolated from an ethyl acetate-soluble part of a methanolic extract of *Taraxacum wallichii*. The structure of **1** was established using NMR, MS, and X-ray crystallographic methods. The ^{13}C NMR data of **2** is also being reported for the first time.

Taraxacum wallichii DC (Compositae) is a variable perennial herb with abundant milky juice in all parts. It is native to temperate and arctic regions particularly in the northern hemisphere[1] and widely distributed in Pakistan at an altitude of 600−3000 m.[2] Plants of the genus *Taraxacum* are used in various indigenous medicines. Roots of some species are reported to have a hepatoprotective effect and are used against visceral diseases.[3] No phytochemical work on *T. wallichii* has been reported. However, other species of *Taraxacum* have yielded a number of sesquiterpene lactones,[4] triterpenoids,[5,6] and glycitols.[7] This note describes the isolation and characterization of a new guaianolide, taraxacin (**1**), along with the known sesquiterpene ketolactone (**2**).[8]



1



2

Taraxacin (**1**) was obtained as yellow powder, which formed crystals in methanol. The formula $C_{15}H_{14}O_3$ was determined through HREIMS (M^+ *m/z* 242.0946, calcd 242.0942), indicating nine degrees of unsaturation. The IR spectrum showed absorption bands at 1740 and 1690 cm^{-1} characteristic of conjugated five-membered lactone and ketone functions, respectively. Intense absorptions in the UV spectrum of **1**, at 335, 270, 250, 231, and 223 nm, indicated the presence of a highly conjugated system.

DEPT experiments resolved the 15 carbon signals in the ^{13}C NMR spectrum into three methyl, one methylene, three methine, and eight quaternary carbons. The three methyl singlets in the ^{1}H NMR (δ 1.98, 2.23, and 2.49) correlated with the carbon signals at δ 8.9 (C-13), 14.3 (C-15), and 22.1 (C-14), respectively, in the HMQC spectrum. In the HMBC spectrum, the cross-peaks of Me-13 (δ 1.98) correlating to C-7, C-11, and C-12; Me-14 (δ 2.49) to C-1 and C-10; Me-15 (δ 2.23) to C-3, C-4, and C-5 confirmed the above-mentioned assignments. The two downfield olefinic methine singlets (δ 6.23 and 6.49) were correlated with the carbons resonating at δ 134.2 (C-3) and 111.1 (C-6), respectively, with the help of an HMQC spectrum. These values were assigned to their respective carbons on the basis of their connectivities [δ 6.23 with C-1, C-2, C-4 and δ 6.49 with C-1, C-5, C-8, C-11] in the HMBC spectrum. The only methylene carbon signal, δ 41.2 (C-9), was correlated with the protons resonating at δ 2.75 and 2.94, which themselves showed HMBC interactions with C-1, C-7, C-8, and C-10. These methylene protons showed cross-peaks in the COSY-45° spectrum with the methine proton at δ 5.05. The proton resonating at δ 5.05 was attached to the carbon resonating at δ 76.9 (C-8), as inferred from the HMQC spectrum. The quaternary carbons appearing downfield in the ^{13}C NMR spectrum at δ 173.4 and 194.2 indicated the presence of carbonyl carbons. They were assigned to C-12 and C-2, respectively, based on their correlations with signals at δ 173.4 (Me-13) and 194.2 (H-3).

All chemical shifts (^{1}H and ^{13}C) of **1** were assigned with the help of HMQC and HMBC experiments. The structure of **1** was confirmed by single-crystal X-ray diffraction. The compound was recrystallized in MeOH, and a suitable crystal was selected for the X-ray diffraction experiment. Unit cell dimensions were found to be $a = 6.2370(10)$, $b = 12.262(2)$, $c = 15.8940(10)$ Å, $\beta = 98.51°$, $V = 1202(3)$ Å^3, $Z = 4$ with the space group $P2_1$ (monoclinic) and two molecules in asymmetric unit. A total of 2637 unique reflections were collected using Cu Kα radiation within the 2θ range 3.5−135°. Of these 1974 reflections were judged observed [$I > 2\sigma(I)$]. The structure was solved by direct methods and refined by full-matrix least-squares techniques to a final discrepancy index of $R = 0.0601$. A computer-generated ORTEP diagram of the final X-ray model of taraxacin is given in Figure 1. Both molecules in the asymmetric unit were found to be identical. The absolute configuration was not determined. Optical rotation ($[\alpha]^{29}_D$ −212°, *c* 0.153, $CHCl_3$) indicated that the compound was enantionmerically pure. The molecule exists in a near planar form, with slight deviations at C-8 and C-9.

Sesquiterpene ketolactone (**2**) was earlier reported as a photo artifact of linderazulene[8] and then as a natural product.[9] This compound was isolated as yellow powder,

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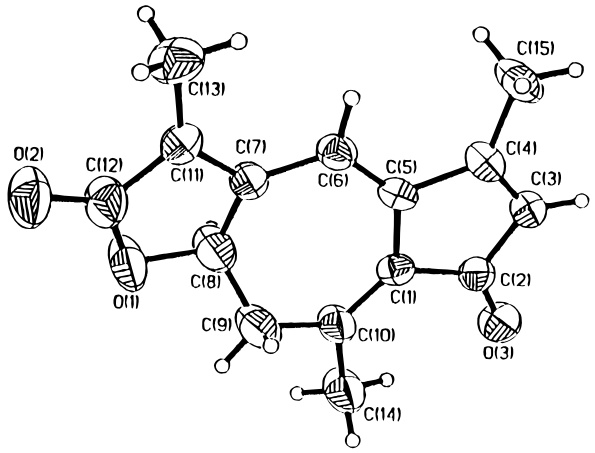

Figure 1. Computer-generated perspective drawing of the final X-ray model of taraxacin (**1**). The configuration shown here is arbitrary.

which was identical with the earlier reported compound in all respects (MP, IR, UV, MS, ^{1}H NMR).[8] The ^{13}C NMR data of **2** is reported here for the first time, and chemical shift assignments (^{1}H and ^{13}C) were made with the help of HMQC and HMBC experiments. Six known compounds were also isolated from this source for the first time: lupeolacetate,[10] β-amyrin,[11] oleonolic acid,[12] ψ-taraxasterol,[13] β-sitosterol,[14] and β-sitosterolglucoside.[14] Structures of known constituents were established by comparing their EIMS and ^{1}H NMR spectra with literature.[8−14]

Experimental Section

General Experimental Procedures. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer at 400 and 100 MHz, respectively. EIMS and HREIMS were recorded on a JEOL-JMS HX-110 spectrometer. IR and UV spectra were recorded on a Shimadzu IR-46 spectrophotometer and a Shimadzu UV-240 spectrophotometer, respectively. Optical rotation was measured on a JASCO DIP-360 polarimeter.

Plant Material. The whole plant material was collected from Islamabad (Pakistan) in February 1999, by one of us (G.A.M) and was identified by Prof. Iftikhar Ali Shah, Department of Pharmacy, Gomal University, D. I. Khan.

Extraction and Isolation. The crushed plant material was soaked in MeOH (3 times 7 days). The combined methanolic extract after concentration under reduced pressure (361.4 g) was extracted with hexane and ethyl acetate, respectively. The ethyl acetate-soluble portion, after evaporation under reduced pressure (57.8 g), was subjected to column chromatography on Si gel. Compounds **1** (39.7 mg) and **2** (37.6 mg) were finally purified by using preparative TLC ($CHCl_3$−MeOH, 9.8:0.2) of the fraction eluted from the initial column with 50% $CHCl_3$−hexane.

Taraxacin (1): yellow needles (MeOH); mp 246 °C; $[\alpha]^{29}_D$ −212° (*c* 0.153, $CHCl_3$); UV (MeOH) λ_{max} (log ϵ) 335 (1.49), 250 (1.33), 223 (0.97) nm; IR ($CHCl_3$) ν_{max} 1740, 1690, 1643−1610 cm^{-1}; EIMS *m*/*z* (rel int) 242 (100) $[M]^+$, 227 (34), 214 (18), 213 (36), 200 (10), 199 (60), 186 (49), 185 (72), 183 (11), 173 (8), 172 (18), 171 (70), 170 (9), 169 (12), 159 (11); ^{1}H NMR (400 MHz, $CDCl_3$) 6.23 (s, H-3), 6.49 (s, H-6), 5.05 (dd, J = 12.5, 3.4, H-8), 2.94 (dd, J = 16.8, 3.4, H-9), 2.74 (dd, J = 16.8, 12.5, H-9), 1.98 (s, Me-13), 2.49 (s, Me-14), 2.23 (s, Me-15); ^{13}C NMR (100 MHz, $CDCl_3$) 128.4 (C-1), 194.2 (C-2), 134.2 (C-3) 143.7 (C-4), 161.5 (C-5), 111.1 (C-6), 154.7 (C-7), 76.9 (C-8), 41.2 (C-9), 147.3 (C-10), 124.3 (C-11), 173.4 (C-12), 8.9 (C-13), 22.1 (C-14), 14.3 (C-15); HREIMS *m*/*z* 242.0946 (calcd for $C_{15}H_{14}O_3$, 242.0942).

Sesquiterpene ketolactone (2): ^{1}H NMR (400 MHz, $CDCl_3$) 6.22 (s, H-3), 6.52 (s, H-6), 6.83 (s, H-9), 2.10 (s, Me-13), 2.69 (s, Me-14), 2.30 (s, Me-15); ^{13}C NMR (100 MHz, $CDCl_3$) 127.0 (C-1), 195.0 (C-2), 132.7 (C-3) 143.4 (C-4), 160.6 (C-5), 114.5 (C-6), 144.7 (C-7), 156.1 (C-8), 116.7 (C-9), 146.0 (C-10), 116.9 (C-11), 170.0 (C-12), 8.4 (C-13), 22.2 (C-14), 14.1 (C-15).

X-ray Crystallography. Taraxacin (**1**) was recrystallized from MeOH by slow solvent evaporation. A crystal with dimensions of 0.25 × 0.25 × 0.30 mm was selected for all crystallographic measurements. Cell dimensions were observed by least-squares fit to $\pm 2\theta$ values of 20 strong reflections measured at room temperature using Cu Kα radiation. All X-ray measurements were carried out on a Nicolet (now Bruker) diffractometer.

Crystal Data for Compound 1. $C_{15}H_{14}O_3$, MW = 242.26, monoclinic, $P2_1$, a = 6.2370(10), b = 12.262(2), c = 15.8940(10) Å, α = 90.0°, β = 98.51°, γ = 90.0°, V = 1202(3) Å^3, Z = 4, D_x = 1.339 Mg/m^3, F(000) = 512, λ (Cu Kα) = 1.54178 Å, μ(Cu Kα) = 0.755 mm^{-1}. The intensity data of all the unique reflections within the 2θ range 3.5−135° were collected at 293(2) K. A total of 2637 unique reflections were recorded, of which 1974 reflections were observed on the basis of $I > 2\sigma(I)$. The structure was solved by direct methods with the use of the program SHELXTL and refined by a full-matrix least-squares on F^2. All the hydrogen atoms were located from difference Fourier maps, and hydrogen parameters were refined. The refinement converged to a final R = 0.0601 (R_w = 0.1645) for 1974 observations and 333 parameters. Electron density in the final difference map was 0.462 and −0.275 e Å^{-3}. Full crystallography data are deposited at the Cambridge Crystallography Data Center, 12 Union Road, Cambridge CB2 1EZ, U.K.

References and Notes

(1) Chadah, Y. R. *The Wealth of India*; Publication and Information Directorate, CSIR: New Delhi, X, p 129.
(2) Ali, S. I.; Nasir, Y. J. *Flora of Pakistan*; Fakhri Printing Press: Karachi, 1972; p 788.
(3) Nadkarni, K. M. *Indian Materia Medica*; Bombay Popular Prakashan Pvt. Ltd.: Bombay, 1972; Vol. 1, p 1196.
(4) Hansel, R.; Kartarahardja, M.; Huang, J. T.; Bohlmann, F. *Phytochemistry* **1980**, *19*, 857−861.
(5) Ageta, H.; Shiojima, K.; Masuda, T.; Lin, T. *Tetrahedron Lett.* **1981**, *22*, 2289−2290.
(6) Santer, J. O.; Stevenson, R. *J. Org. Chem.* **1962**, *27*, 3204−3208.
(7) Ezekiel, A. D.; Overend, W. G.; Williams, N. R. *Tetrahedron Lett.* **1969**, 1635−1638.
(8) Alpertunga, B.; Imre, S.; Cowe, H. J.; Cox, P. J.; Thomson, R. H. *Tetrahedron Lett.* **1983**, *24*, 4461−4462.
(9) Li, M. K. W.; Scheuer, P. J. *Tetrahedron Lett.* **1984**, *25*, 2109−2110.
(10) Ageta, H.; Shiojima, K.; Lin, T. *Tetrahedron Lett.* **1981**, 2289−2290.
(11) Reynolds, F.; Mclean, S.; Poplawski, J.; Enriquez, P. G.; Escobar, L. I. *Tetrahedron* **1986**, 3419−3428.
(12) Heupel, R. C. *Phytochemistry* **1985**, *24*, 2929−2937.
(13) Gonzalez, A. G.; Amaro, J.; Fraga, B. M.; Luis, J. G.; Fayos, J.; Perales, A.; Mendez, M. P. *Phytochemistry* **1984**, *23*, 2079−3080.
(14) Sadikum, A.; Aminah, I.; Ismail, N.; Ibrahim, P. *Nat. Prod. Sci.* **1996**, *2*, 19−23.

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