Two New Eudesmane Alcohols from *Jasonia glutinosa*

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Z. Naturforsch. **55c,** 693–696 (2000); received April 3/May 15, 2000

Asteraceae, Eudesmane Alcohols, *Jasonia glutinosa*

Two new sesquiterpene alcohols have been isolated from the aerial parts of *Jasonia glutinosa* D. C. The structure of these sesquiterpenes were characterized by 1D and 2D NMR techniques (DQCOSY, TOCSY, NOESY, HMQC and HMBC) as (11*R*)-eudesm-4-en-11,12-diol and (11*R*)-eudesmane-5α,11,12-triol.

Introduction

Jasonia glutinosa D.C, (*Chiliadenus saxatilis*, Cass.) (Brullo, 1979) (*Chiliadenus glutinosus* (L) Fourr.) (Greuter *et al.*, 1989; Merxmüller *et al.*, 1977) is an annual plant occurring in the Mediterranean littoral area of the Iberian Peninsula, South of France and Malta. It is named "rock tea" and it is used in spanish traditional medicine as an antispasmodic, anticatarrhal, antihypertensive, hemostatic, antiseptic, antifungic and antiinflamatory drug (Arteche *et al.*, 1998).

Previous phytochemical investigations on *J. glutinosa* have revealed the presence of sesquiterpene alcohols (Pacual *et al*, 1978; Villaescusa-Castillo *et al.*, 1995; Pascual *et al.*, 1980). We report here the isolation and characterization of two new eudesmane alcohols from this species.

Results and Discussion

The acetone/water extract of aerial parts of *J. glutinosa* was fractionated by a silica gel column to give two fractions, from which further purification by medium pressure liquid chromatography (MPLC) yielded compounds **1** (5 mg) and **2** (21 mg).

The mass spectrum of **1** gave a $[M]^+$ ion at *m/z* 238, corresponding to a molecular formula $C_{15}H_{26}O_2$. The high resolution ^{1}H-NMR spectrum in methanol-d_4 contained an AB system centered at 3.44 (J = 11.2), characteristic of a CH_2 group linked to an oxygen atom, a multiplet at δ 2.71 and three methyl singlets (δ 1.60, 1.08, and 1.02), being the first of them slightly broadened by long range couplings. These couplings and the chemical shift strongly suggested the presence of a methyl group attached to a double bond.

The ^{13}C-NMR spectrum of **1** gave 15 signals, and confirmed the occurrence of a double bond (peaks at δ 136.2 and 125.4). The absence of ethylenic protons indicated that it was a tetra-substituted double bond. The multiplicities of the individual ^{13}C peaks, determined using the DEPT (distortionless enhancement by polarization transfer) pulse sequence, indicated the presence of three methyl, seven methylene, and one methine groups, and four quaternary carbons. The assignment of proton and carbon signals was achieved from DQCOSY and 2D- TOCSY (HOHAHA) (mixing time = 80 ms) experiments, and also from ^{1}H-^{13}C heteronuclear multiple quantum (HMQC) and multiple bond correlations (HMBC). The data obtained have been gathered in Table I. It was also possible the measurement of some of the coupling constants. For instance, H-7 contained two large couplings (J =12.5 Hz), which indicated an axial proton. All these data, together with the rest of spectroanalytical results, allowed to propose the structure of **1** as (11*R*)-eudesm-4,5-en-11,12-diol.

The structure of compound **1**, now found in *J. glutinosa*, has been reported as obtained in intermediate steps in partial syntheses of Kudtdiol and Kudtriol (Pascual *et al.*, 1980; Harapanhalli, 1988). The $[\alpha]_D$ and ^{1}H-NMR spectral values were prac-

0939–5075/2000/0900–0693 $ 06.00

Table I. ^{1}H- and ^{13}C-NMR data (δ, *J* Hz) for compounds **1** and **2**.

	1[a]		**2**[a]		**2**[b]	
Atom	^{1}H	^{13}C	^{1}H	^{13}C	^{1}H	^{13}C
1	1.28 1.48	41.5	1.64 ($J_{1a,1e}=J_{1a,2a}=13.6$) 0.95 ($J_{1a,2e}=3.5$)	35.8	1.54 ($J_{1a,1e}=J_{1a,2a}=13.3$) 1.01 ($J_{1a,2e}=3.4$)	34.8
2	1.58 1.52	20.2	1.77 ($J_{2a,2e}=J_{2a,3a}=13.6$) 1.37 ($J_{2a,3e}=4.0$)	18.2	1.70 ($J_{2a,3a}=13.6$) 1.38 ($J_{2e,3a}=5.4$)	17.0
3	1.97 1.87	34.2	2.16 ($J_{3a,3e}=13.6$) 1.25	29.1	2.01 ($J_{3a,3e}=13.6$) 1.30 ($J_{3a,4}=4.9$)	28.1
4	–	125.3	1.63	42.6	1.62	41.3
5	–	136.2	–	76.8	–	75.8
6	1.70 ($J_{6a,6e}=J_{6a,7}=12.5$) 2.71 ($J_{6e,7}=3.2$)	26.4	1.86 ($J_{6a,6e}=J_{6a,7}=13.0$) 1.24	33.4	1.79 ($J_{6a,6e}=J_{6a,7}=12.7$) 1.28 ($J_{6e,7}=4.0$)	32.1
7	1.44 ($J_{7,8a}=12.5$)	46.9	2.13	39.6	2.13 ($J_{7,8a}=12.7$) ($J_{7,8e}=4.0$)	38.9
8	1.57 1.44	24.5	1.45 ($J_{8a,9a}=J_{9a,9e}=12.4$) 1.45 ($J_{8a,9e}=J_{8e,9e}=3.5$)	22.6	1.33 1.42	22.0
9	1.55 1.23	43.6	1.81 ($J_{8e,9a}=5.7$) 0.92	38.9	1.75 0.96	37.8
10	–	35.6	–	37.6	–	36.7
11	–	75.5	–	75.4	–	74.7
12	3.46 (J = 11.2) 3.42	69.2	3.40 (J = 11.1) 3.43	69.1	3.54 (J = 11.0) 3.41	68.8
13	1.08	20.2	1.12	21.5	1.11	19.9
14	1.02	25.1	1.07	22.3	1.04	21.7
15	1.60	19.4	1.04 ($J_{4,Me}=7.5$)	17.2	1.02 ($J_{4,Me}=7.5$)	16.8

[a] In CD_3OD. [b]In $CDCl_3$.

tically identical to those reported for that intermediate (Pascual *et al.*, 1980) (see experimental).

The MS spectrum of **2** showed the molecular ion $[M]^+$ at *m/z* 256, in agreement with a molecular formula $C_{15}H_{28}O_3$. The 500 MHz ^{1}H-NMR spectrum in methanol-d_4 contained two methyl singlets at δ 1.07 and 1.12 ppm. A doublet (3H) located at δ 1.04 suggested the presence of a third methyl group coupled with a proton. As in **1**, the occurrence of a -CH_2OH group was inferred from the presence of two doublets at δ 3.43 and 3.40 (J = 11.1 Hz). Assignment of most of the protons was achieved using DQCOSY and TOCSY (mixing time = 80 ms) techniques, although heavy overlapping of protons precluded a complete assignation.

The ^{13}C-NMR spectrum gave 15 peaks. The multiplicities of the individual ^{13}C peaks (DEPT pulse sequence), indicated the presence of three methyl, seven methylene, and two methine groups, and three quaternary carbons. Assignment af the rest of protons and all carbons was achieved from HMQC and HMBC experiments (see Table I). The long range ^{1}H-^{13}C connectivities observed in the HMBC spectrum allowed to deduce an esqueleton related to that of eudesmane. We then tried to measure most of the coupling constants, in order to determine the conformation of the rings, running parallel experiments in $CDCl_3$. In this solvent, protons H-1a, H-3a, H-4, and H-7 did not overlapped. A series of pulse-shaped NOE experiments in both solvents allowed the measurement of most of the coupling constants, taking advantage of the strong NOE's between geminal protons. The coupling constants for a given proton, measured in both solvents, varied only in the range ± 0.3 Hz, which indicated that no significant conformational modification occurred when the solvent was changed from CD_3OD to $CDCl_3$ hence, for conformational studies of the rings we can take the values obtained in one solvent to complement those found only in the other (see Table I). From the coupling constants, it can be deduced that H-4 is equatorial ($J_{3a,4}$ = 4.9, $J_{3e,4}$ = 3.8) hence Me-15 is axial. Proton H-7 is axial ($J_{6a,7}$ = $J_{7,8a}$ = 12.7 Hz). In addition, NOESY experiments (mixing time = 400 ms) gave crosspeaks H-2a/Me-14, H-2a/Me-15, H-3a/H-4, H-6a/Me-14, H-6a/Me-

15, H-7/H-6e, and H-7/H-8e. All those results permit to propose for compound **2** the structure and conformation shown in Fig. 1.

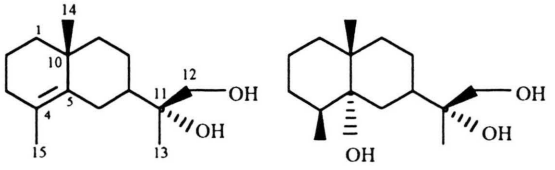

Fig. 1. Structures for compounds **1** and **2**.

Experimental

MS spectra were obtained in a Hewlett Packard 5988 A mass spectrometer. Analytical TLC was performed on precoated Si gel aluminum plates (Kieselgel G-60 F-254, 0.25 mm, Merck) using $CHCl_3$/MeOH (95/5 v/v) for compound **1** and pure EtOAc for compound **2**, and visualized with 1% vanillin in MeOH-H_2SO_4 (50:50). Optical rotations were measured on a Perkin-Elmer 241 polarimeter, using a sodium lamp operating at 598 nm. 1D and 2D NMR spectra were recorded on a Varian UNITY 500 spectrometer for $CDCl_3$ or CD_3OD solutions at 30 °C. (proton: 500 MHz; carbon: 125 MHz); the residual chloroform or methanol peaks (δ 7.24 and 3.30 for proton and δ 77.0 and 49.0 for carbon, respectively) were used as references. The standard pulse sequences from the Varian software were used for homonuclear and heteronuclear correlation experiments (DQCOSY, TOCSY, NOESY, HMQC and HMBC).

Collection, extraction and isolation

The aerial parts of *J. glutinosa* were collected in San Andrés del Congosto (Guadalajara, Spain), in July 1997 and was identified by Dr. C. Bartolomé, Departamento de Biología Vegetal (Facultad de Ciencias, Universidad de Alcalá, Madrid, Spain. A voucher specimen was deposited at the Herbarium of the Universidad de Alcalá.

The dried and powdered aerial parts (500 g), were extracted with acetone/water (30/70 v/v) (5 l; 24 hr.), at room temperature. The residue was further extracted with pure acetone (4 l) under the same conditions.

The acetone/water extract (4 g) was subjected to flash CC (FLASH 40^{TM} + SIM version 2.0 [12/96] 4 × 15 cm) over silica gel, and eluted with a $CHCl_3$/MeOH step gradient. The fraction obtained after elution with pure chloroform, yielded compound **1** (5 mg). The pure acetone extract (8 g) was purified by consecutive flash CC (FLASH 40^{TM} + SIM version 2.0 [12/96] 4 × 15 cm) and eluted with $CHCl_3$/MeOH (99/1 v/v) by an isocratic system, including an EtOAc/toluene step gradient. The fraction obtained after elution with EtOAc/toluene (35/65 v/v) was further submitted to MPLC (RP-18; 0.026–0.040 mm; Merck; 3 × 40 cm; MeOH (45% to 100%). Elution with 70% MeOH yielded 21.1 mg of compound **2**.

(11R)-Eudesm-4-en-11,12-diol **(1)**

Gum, *m/z* 238 $[M]^+$, $C_{15}H_{26}O_2$; $[\alpha]_D$ +120° (MeOH, *c* 0.02); ^{1}H-NMR ($CDCl_3$, TMS as internal standard) δ: 3.60 (d, 1H, H-12a) and 3.41 (d, 1H, H-12b; AB system, J = 11.0 Hz), 1.59 (s, 3H, Me-15), 1.13 (s, 3H, Me-13), 1.01 (s, 3H, Me-14). ^{1}H- and ^{13}C-NMR data (CD_3OD): see Table I.

(11R)-Eudesmane-5α,11,12-triol **(2)**

White solid, mp 49–51 °C; *m/z* 256 $[M]^+$, $C_{15}H_{28}O_3$; $[\alpha]_D$ +162.5° (MeOH, *c* 0.04); IR: ν_{max} (cm^{-1}) 3392, 2940, 1049, 1032, 992; ^{1}H and ^{13}C NMR data: see Table I.

Acknowledgements

We are grateful to Dr. M. C. de la Torre for her kind help in the determination of α_D values, Universidad de Alcalá (012/95; 045/96 and E038/97), PICASSO (Acciones integradas Hispano-Francesas; HF-211 & 98B), Ministerio de Educación y Cultura, Ministerio de Sanidad (FISS 9471671), and Comunidad Autónoma de Madrid, (C101/91) for supporting this research.

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