Pergamon

0031-9422(95)00377-O

Phytochemistry, Vol. 40, No. 4, pp. 1193–1195, 1995

0031-9422/95 $9.50 + 0.00

TWO SESQUITERPENOIDS, LUCINONE AND GLUTINONE, FROM *JASONIA GLUTINOSA*

LUCINDA VILLAESCUSA CASTILLO,* ANA MARIA DIAZ LANZA,* ROBERT FAURE,† LAURENT DEBRAUWER,‡ RIAD ELIAS§ and GUY BALANSARD§¶

* Laboratoire de Farmacognosia, Facultad de Farmacia, Universidad de Alcala de Henares, Madrid, Spain; † URA 1411, Université d'Aix-Marseille III, Avenue Escadrille Normandie Niemen, 13397 Marseille cedex 3, France; ‡ INRA Centre de Recherche de Toulouse, Laboratoire des Xénobiotiques, 180 Chemin du Tournefeuille, PB 3, 31931 Toulouse, France; § Laboratoire de Pharmacognosie, Faculté de Pharmacie, 27 Bd Jean Moulin, 13385 Marseille cedex 5, France

(*Received* 18 *January* 1995)

Key Word Index *Jasonia glutinosa*; *Chiliadenus glutinosus*; Asteraceae; lucinone; glutinone; 5β,11,12-trihydroxy-iphionan-4-one; 2-[5′-(2′-oxopentyl)]-2-methyl-5-(1′-hydroxy-1′-methylethanol)-cyclohexanone; ^{1}H NMR; ^{13}C NMR; 2D NMR.

Abstract– Two new sesquiterpenoids – lucinone (**1**) and glutinone (**2**) – isolated from the aerial parts of *Jasonia glutinosa* have been characterized by 1D and 2D NMR techniques. The complete structure of these sesquiterpene compounds have been determined as 5β,11,12-trihydroxy-iphionan-4-one and 2-[5′-(2′-oxopentyl)]-2-methyl-5-(1′-hydroxy-1′-methylethanol)-cyclohexanone, respectively.

INTRODUCTION

Jasonia glutinosa D. C. (*Chiliadenus saxatilis*, Cass.) [1] *Chiliadenus glutinosus* (L.) Fourr. [2], Asteraceae is an annual medicinal plant occurring in the Mediterranean littoral area of the Iberian Peninsula [3], South of France and Malta [4]. It is used in traditional medicine as an antispasmodic drug [3]. Until now, only sesquiterpene alcohols have been investigated [5–7]. In the present paper we report the isolation and structural elucidation of two new sesquiterpenoids.

RESULT AND DISCUSSION

The FAB MS spectrum of lucinone (**1**) showed the molecular ion at m/z 271 $[M - H^+]^+$ in agreement with a molecular formula of $C_{15}H_{26}O_4$. The 400 MHz ^{1}H NMR spectrum shows two singlets at δ0.96 and 1.09 ppm which were attributed to two quaternary methyl groups. A third singlet signal (3H) located at 2.20 ppm was assigned to a carbonyl methyl group. Close inspection of the remaining ^{1}H NMR resonances confirmed the presence of methylene protons linked to an oxygen-bearing carbon (an AB quartet (J = 11 Hz) at 3.46 and 3.43 ppm) and a deshielded signal at δ3.41 ppm (1H, *dd*, J = 7.9, 10.2 Hz). In the ^{13}C NMR spectrum the occurrence of a carbonyl function was supported by the resonance at 213.8 ppm. The multiplicities of the individual ^{13}C peaks determined using the DEPT pulse sequence, indicated four quaternary carbons, three methyl groups and six methylene and two methine resonances. It can be concluded from these data that compound **1** must contain two rings.

The structural determination of lucinone (**1**) can be easily accomplished using a combination of homonuclear and both direct and long-range heteronuclear chemical shift correlation experiments.

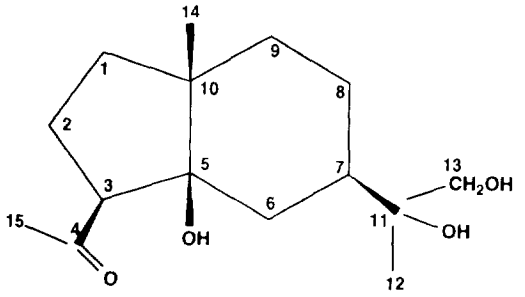
One-bond proton-carbon chemical shift correlation was established using the proton detected, C, H correlation technique HMQC [8] and providing the identities of the direct responses. Utilizing the long-range heteronuclear multiple quantum bond connectivity (HMBC) diagram [9], structural fragments can be determined.

Thus, the following substructures **A1**, **B1** and **C1** were deduced from the connectivities observed between the proton methyl shifts and carbons α and β to these groups.

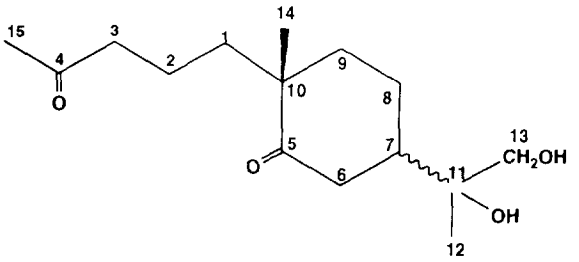
Finally, analysis of long-range heteronuclear correlation responses for the other ^{1}H resonances in conjunction with the proton intercoupling network determined from the homonuclear ^{1}H–^{1}H correlation COSY [10, 11] permits the inclusion of other groups in structural fragments **A1**, **B1** and **C1**. From this information (Table 1), the structure of lucinone (**1**) was deduced to be 5β,11,12-trihydroxy-iphionan-4-one. Since these ^{13}C NMR data were consistent with those concerning similar iphionan-type sesquiterpenoids [12], we supposed the same stereochemistry at C-3, C-5, C-7 and C-10 positions for **1**.

The molecular formula for **2** was found to be $C_{15}H_{26}O_4$, by FAB MS (m/z 271) $[M - H^+]^+$. Its

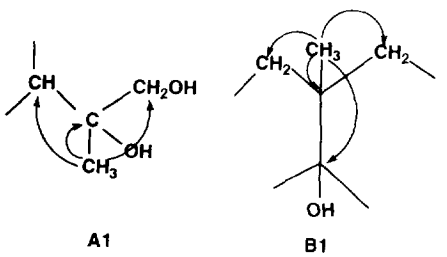
¶ Author to whom correspondence should be addressed.



Lucinone (1)



Glutinone (2)



^{1}H NMR spectrum indicates three methyl resonating as singlets (δ1.11, 1.12, and 2.11 ppm) and two protons on an oxygen-bearing carbon (AB quartet, J = 10.8 Hz, δ3.56 and 3.41 ppm). Moreover, the methyl singlet at 2.11 ppm can be ascribed with certainty to a methyl carbonyl group. The ^{13}C NMR data revealed the presence of two carbonyl signals (δ215.89 and 209.27 ppm). The multiplicities of the ^{13}C NMR peaks (4C, 3CH_3, 7CH_2 and 1CH) and the above results suggested a monocyclic structure for **2**.

The molecular framework and the complete ^{1}H and ^{13}C chemical shift assignments (Table 1) of glutinone (**2**) were deduced, as for lucinone (**1**) on the basis of the concerted application of two-dimensional experiments. Considerations of the various connectivities (Fig. 1) in conjunction with the inferences drawn from the conventional 1D NMR spectra gave 2-(5′-(2′-oxopentyl))-2-methyl-5-(1′-hydroxy-1′-methylethanol)-cyclohexanone as identification of compound **2**.

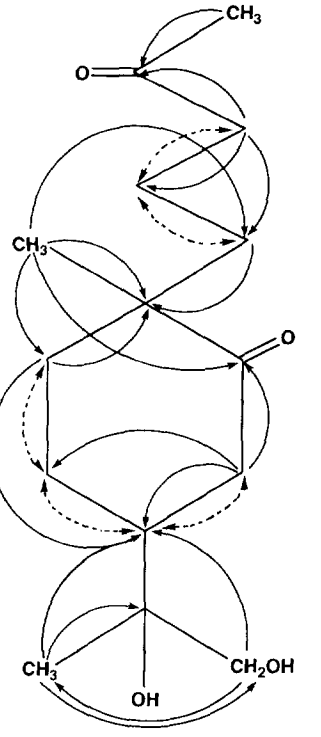


Fig. 1. Selected long-range C. H connectivities from the proton to the protonated or quaternary carbon to which the arrow points (→) and molecular ^{1}H, ^{1}H connectivities (-----) observed for glutinole (**2**).

EXPERIMENTAL

Jasonia glutinosa plants were collected in July 1993 in San Andres del Congosto (Guadalajara, Spain) and a voucher specimen is kept in the Department of Vegetal Biology (Faculty of Sciences, University of Alcala de Henares, Madrid, Spain).

Extraction and isolation. The dried aerial parts (1 kg) was extracted with MeOH (10 ml g^{-1}; 48 hr) at room temp. The MeOH extract (144 g) was subjected to solvent partitioning between *n*-hexane and 5% aq. MeOH. The aq. MeOH portion was further extracted with CH_2Cl_2, 25 g of the CH_2Cl_2 fraction was subjected to CC over silica (Kieselgel G-60, 0.040–0.063 mm; Merck. The fraction obtained after elution with CH_2Cl_2–MeOH (97:3) was further submitted to MPLC (RP-18; 0.026–0.040 mm; Merck; MeOH (50–100%)). Elution with MeOH 60% yielded compounds **1** (59.5 mg) and **2** (95 mg). The possibility of aldol condensation was unlikely since all procedures were conducted in neutral conditions.

Analytical TLC. This was performed on precoated Si gel plates (Kieselgel G-60 F-254, 0.25 mm, Merck) using the following solvent system EtOAC 100% and reverse phase plates (RP-18 $F_{254}S$, Merck) using MeOH 75% as solvent. Visualization of the TLC plates was achieved with a long wavelength UV lamp and H_2SO_4 spray reagent.

Table 1. ^1H and ^{13}C NMR chemical shift* assignments for lucinone (**1**) and glutinone (**2**)

	1			2		
	Group†	^1H‡	^{13}C‡	Group†	^1H‡,§	^{13}C‡
1	CH_2	1.84 and 1.37	38.55	CH_2	1.42 and 1.37	37.35
2	CH_2	2.14 and 1.86	23.52	CH_2	1.51 and 1.44	18.30
3	CH	3.41	57.29	CH_2	2.41	44.37
4	C		213.80	C		209.27
5	C		85.05	C		215.79
6	CH_2	2.09 and 1.41	32.54	CH_2	2.44 and 2.36	38.91
7	CH	1.83	42.31	CH	1.89	45.25
8	CH_2	1.52 and 1.25	23.96	CH_2	1.71 and 1.59	22.35
9	CH_2	1.40	37.43	CH_2	1.74 and 1.58	36.42
10	C		47.35	C		47.39
11	C		74.99	C		73.90
12	CH_3	1.09	20.81	CH_3	1.12	20.50
13	CH_2	3.46 and 3.43	69.16	CH_2	3.56 and 3.41	68.26
14	CH_3	0.96	19.03	CH_3	1.11	23.23
15	CH_3	2.20	31.38	CH_3	2.11	29.99

*In ppm from TMS: measured in CD_3OD for **1** and $CDCl_3$ for **2**.

†Determined from DEPT spectra.

‡Information obtained from concerted application of homonuclear and heteronulcear chemical shift correlations.

§δOH: 2.15 ppm.

FAB MS. FAB MS spectrum was obtained on NERMAG R10-10H mass spectrometer in the positive mode in a glycerol matrix.

NMR. All 1D and 2D NMR spectra were recorded on a Bruker AMX-400 spectrometer in $CDCl_3$ or CD_3OD solns (^1H at 400 MHz; ^{13}C at 100.61 MHz, TMS as std in both measurements). Standard Bruker pulse sequences were used for homonuclear and heteronuclear correlation experiments (COSY, HMQC and HMBC). For other experimental details see Ref. [13].

Lucinone (**1**). 5β,11,12-Trihydroxy-iphionan-4-one. Gum; FAB MS: $m/z = 271$ $[M - H^+]^+$; ^1H NMR, ^{13}C NMR and 2D NMR (CD_3OD) Table 1.

Glutinone (**2**). 2-[5′-(2′-Oxopentyl)]-2-methyl-5-(1′-hydroxy-1′-methylethanol)-cyclohexanone. FAB MS: $m/z = 271$ $[M - H^+]^+$; ^1H NMR, ^{13}C NMR and 2D NMR ($CDCl_3$) (Table 1).

REFERENCES

1. Brullo, S. (1979) *Webbia*. **34**, 289.
2. Greuter, W., Burdet, H. M. and Long, G. (1989) in *Med. Checklist* (Vol. 4: Compositae), p. 458. Conser. Jard. Bot. Genève, Geneva.
3. Font-Quer, P. (1982) in *Plantas Medicinales*, p. 790. El Dioscorides Renovado.
4. Tutin, T. G. (1976) in *Fl. Europ.* (Tutin, T. G., ed.), Vol. 4, p. 138. Cambridge University Press, Cambridge.
5. De Pascual, T. J., Barrero, A. F., San Feliciano, A., Grande, M. and Medarde, M. (1978) *Tetrahedron Lett.* **43**, 4141.
6. De Pascual, T. J., Barrero, A. F., San Feliciano, A. and Medarde, M. (1980) *Phytochemsitry* **19**, 2155.
7. De Pascual, T. J., Barrero, A. F., Medarde, M. and San Feliciano, A. (1982) *Ann. Quim.* **78**, 317.
8. Bax, A. and Subramanian, S. (1986) *J. Magn. Res.* **67**, 565.
9. Bax, A. and Summers, M. F. (1986) *J. Am. Chem. Soc.* **108**, 2093.
10. Aue, W. P., Bartholdi, E. and Ernst, R. R. (1976) *J. Chem. Phys.* **64**, 2229.
11. Nagayama, K., Kumar, A., Wüthrich, K. and Ernst, R. R. (1980) *J. Magn. Res.* **40**, 321.
12. El-Ghazouly, M. G., El-Sebakhy, N. A., El-Din, A. A. S., Zdero, C. and Bohlmann, F. (1987) *Phytochemistry* **26**, 439.
13. Raharivelomanana, P., Bianchini, J. P., Faure, R., Cambon, A. and Azzaro, M. (1995) *Magn. Res. Chem.* (in press).