Pergamon

PII: S0031-9422(98)00293-3

Phytochemistry Vol. 49, No. 8, pp. 2425–2427, 1998

Printed in Great Britain
0031-9422/98/$ - see front matter

EUDESMANOLIDE FROM *CENTAUREA GRANATA*

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(*Received in revised form* 9 *March* 1998)

Key Word Index—*Centaurea granata*; Compositae; sesquiterpene lactones; eudesmanolides.

Abstract—Investigation of the aerial parts of *Centaurea granata* afforded, in addition to two known polymethoxylated flavones, a new eudesmanolide. The structure of the new compound was elucidated by spectroscopic methods as 8α-hydroxy-11β,13-dihydro onopordaldehyde.

INTRODUCTION

In continuation of our previous chemical investigation of the genus Centaurea [1–3], we have investigated *Centaurea granata L.* We now report on the isolation and structural elucidation of a new eudesmanolide together with two known flavones.

RESULTS AND DISCUSSION

Column chromatography of the chloroform-soluble portion of a methanol extract of the aerial parts of *C. granata* afforded two flavones and a sesquiterpene lactone. The flavones were identified [4] as 5-hydroxy-6,7,3′,4′-tetramethoxyflavone (**1**) and 5,3′-dihydroxy-6,7,4′-trimethoxyflavone (**2**). The position of methoxyl groups in these compounds followed from the mass [5] and UV [6] spectral data as well as by ^{1}H NMR [7]. The mass spectrum of the new compound **3** showed the quasi-molecular ion $[M + NH_4]^+$ at *m/z* 284 (DCI/NH_3) and ions at *m/z* 267 (2%) $[MH]^+$, 238 (20%) $[M - CO]^+$ and 220 (100%) $[M - CO - H_2O]^+$ (DEI). These data agreed with a molecular formula $C_{15}H_{22}O_4$. The ^{1}H NMR spectrum (Table 1) exhibited a typical triplet at δ 3.79 for H-6 and a double triplet at δ 3.95 for H-8 indicating the presence of oxygenated functions at C-6 and C-8. In addition the coupling patterns and the magnitude of the coupling constants of H-5 to H-8 were in agreement with *trans* disposition of H-5/H-6, H-6/H-7 and H-7/H-8. The same spectrum exhibited an angular methyl signal at δ 0.98 which suggested that this compound has a eudesmanolide-type skeleton and an aldehyde proton signal (doublet) at δ 9.55 which could be at C-4. The α orientation of the aldehyde group could be deduced from the value of the coupling constant (4 Hz) between H-4 and H-15 which is in agreement with an axial position for H-4 [8]. The triplet at δ 1.75 (J = 11 Hz) which may be attributed to H-5 confirmed the β-position of H-4. The doublet at δ 1.36 (J = 7 Hz) was attributed to H-13. The *dq* at δ 2.52 (J = 12; 7 Hz) was attributed to H-11 and then the configurations at C-5, C-6, C-7, C-8, and C-11 followed from the couplings observed. In the ^{13}C NMR spectrum (Table 1), the signals at 203.20; 177.96; 79.20 and 68.32 ppm were assigned to C-15 (aldehyde 1730 cm^{-1} in the IR spectrum), C-12 (γ-lactone 1780 cm^{-1} in the IR spectrum), C-6 and C-8 respectively.

All these assignments were confirmed by ^{1}H-^{1}H COSY, ^{1}H-^{13}C COSY, DEPT experiments and are in good agreement with literature data for similar eudesmanolides [8–13]. In an HMBC (400 MHz) experiment optimized for an 8 Hz long-range coupling, a correlation between H-6 and C-12 was found. This correlation and the chemical shifts of H-6, H-8, C-6 and C-8 indicated a C-6 lactonized eudesmanolide with an hydroxyl group at C-8. Therefore, compound **3** is 8α-hydroxy-11β,13-dihydro onopordaldehyde [13].

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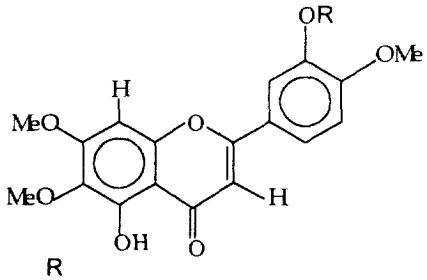
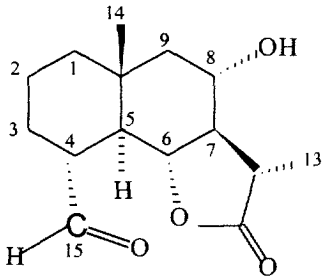


R

1 CH_3

2 H



3

EXPERIMENTAL

Plant material

Centaurea granata was collected from El-kala in eastern Algeria and authenticated by Dr. Mohamed Kaâbache from the Department of Biology (University of Setif, Algeria). A voucher specimen is deposited in the Herbarium of Research Unit of Chemistry, University of Constantine. under n° 05/1988/CCG10.

Extraction and isolation of the compounds

Air-dried and powdered aerial parts (175 g) were soaked in MeOH (1,5 l). The MeOH extract was concentrated and the residue dissolved in H_2O (70 ml). The sol. was treated with $Pb(OAc)_2$ under stirring and filtered.

The yellow coloured filtrate was extracted with $CHCl_3$ (3 × 30 ml). The extract was dried with Na_2SO_4 and then concd. to a gum (1 g) [14]. The gum (1 g) was dissolved in a minimum amount of $CHCl_3$ and the soln. chromatographed over a silica gel (230–400 mesh) column with $CHCl_3$ to give **1** and **2**. CC was achieved with hexane–$CHCl_3$–EtOAc (1:1:1) to give **3**.

Table 1. ^1H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectral data of compound **3** [$CDCl_3$ + 1 drop MeOH (d_4), TMS as int. standard and (last col.) $CDCl_3 + C_6D_6$, 3:1]

H		C		
1	*	1	26.09	25.08
1′	*	2	19.30[a]	19.30[b]
2	*	3	40.43	40.39
2′	*	4	48.89	48.84
3	*	5	48.39	48.29
3′	*	6	79.20	79
4	2.45 *m*	7	59.20	59.10
5	1.75 *t*	8	68.32	68.54
6	3.79 *t*	9	51.50	51.15
7	1.68 *m*	10	35.14	35.07
8	3.95 *dt*	11	41.21	41.13
9	1.38 *m*	12	177.96	178
9′	1.86 *dd*	13	14.31	14.33
11	2.52 *dq*	14	19.30[a]	19.22[b]
13	1.36 *d*	15	203.20	202.09
14	0.98 *br. s*			
15	9.55 *d*			
OH	3.47 *s*			

* Obscured multiplets
[a] Superposition of C-2 and C-14
[b] Assignments may be interchanged
J (Hz): 4,15 = 8,9′ = 4; 4,5 = 5,6 = 6,7 = 7,8 = 8,9 = 11; 7,11 = 12; 9,9′ = 13.

8α-*Hydroxy*-11β,13-*dihydro onopordaldehyde* (**3**)

White crystals, mp 235°; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600 (OH), 1780 (γ-lactone), 1730 (aldehyde); EIMS *m/z* (rel. int.): 267 $[MH]^+$ (2), 266 $[M]^+$ (0.5), 238 $[M-28]^+$ (20), 220 $[M-CO-H_2O]^+$ (100), 205 (40), 147 (62); DCIMS (NH_3) *m/z* (rel. int.): 284 $[MNH_4]^+$ (100); UV λ_{max}^{MeOH} nm: 273 (97); $[\alpha]_D^{20}$ + 20° (MeOH, *c* 0.1)

REFERENCES

1. Benayache, F., Benayache, S., Medjroubi, K., Massiot, G., Aclinou, P., Drozdz, B. and Nowak, G., *Phytochemistry*, 1992, **31,** 4360.
2. Medjroubi, K., Benayache, F., Benayache, S., Akkal, S., Khalfallah, N. and Aclinou, P., *Phytochemistry*, 1997, **45,** 1449.
3. Akkal, S., Benayache, F., Benayache, S. and Jay, M., *Biochemical Systhematics and Ecology*, 1997, **25**(4), 361.
4. Mabry, T. J., Markham, K. R. and Thomas, M. B., *The Systematic Identification of Flavonoids*. Springer, New York, 1970.
5. Goudard, M., Favre-Bonvin, J., Lebreton, P. and Chopin, J., *Phytochemistry*, 1978, **17,** 145.
6. Voirin, B., *Phytochemistry*, 1983, **22,** 2107.
7. Markham, K. R., *Techniques of Flavonoid Identification*. Academic Press, London, 1982.
8. Rustaiyan, A., Ahmadi, B., Jakupovic, J. and Bohlmann, F., *Phytochemistry*, 1986, **25,** 1659.
9. Shimizu, S., Miyaze, T., Ueno, A. and Usmanghani, K., *Phytochemistry*, 1989, **28,** 3399.

10. Miski, M., Meriçli, A. H. and Mabry, T. J., *Phytochemistry*, 1988, **27,** 1417.
11. Mahmoud, Z., El-Masry, S., Amer, M., Ziesche, J. and Bohlmann, F., *Phytochemistry*, 1983, **22,** 1290.
12. Da Silva, A. J. R., Garcia, M., Baker, P. M. and Rabi, J. A., *Organic Magnetic Resonance*, 1981, **16**(3), 234.
13. Rustaiyan, A., Nazarians, L. and Bohlmann, F., *Phytochemistry*, 1979, **18,** 879.
14. Drozdz, B. and Piotrowski, J., *Polish Journal of Pharmacology and Pharmacy*, 1973, **25,** 91.