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STRUCTURE AND STEREOCHEMISTRY OF MELITENSIN, AN ELEMANOLIDE FROM *CENTAUREA ASPERA* VAR. *STENOPHYLLA*

AMPARO TORTAJADA, MARIA-TERESA PICHER, MARIA-MERCEDES REVENTOS* and JOSE-MARIA AMIGO*

Departamento de Química Orgánica, Facultad de Química, Universitat de València, Campus de Burjassot, 46100-València, Spain, *Sección de Cristalografía y Mineralogía, Departamento de Geología, Universitat de València, Campus de Burjassot, 46100-València, Spain

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Key Word Index—*Centaurea aspera* var *stenophylla*, Compositae; melitensin, elemanolide; sesquiterpene lactone, X-ray structure analysis

Abstract—A crystalline compound, melitensin, obtained from an extract of *Centaurea aspera* var. *stenophylla* was shown to be 8α, 15-dihydroxyelema-1,3-6α,12-dien-olide by X-ray analysis. The molecular structure of melitensin was solved with orthorhombic space group $P2_12_12_1$, $a = 8.469(5)$, $b = 10.769(5)$, $c = 16.452(5)$Å for $Z = 4$ by direct methods and refined to a final R of 0.08 for 1493 observed reflections

INTRODUCTION

Melitensin is a crystalline compound isolated by González *et al.* [1, 2] from *Centaurea melitensis* some time ago, and recently by us [3] from *Centaurea aspera* L. subsp. *stenophylla* (Dufour) Nyman. Although the ^{1}H NMR spectra favour the structure of 8,15-dihydroxyelema-1,3-dien-olide, other structures could not be definitively eliminated and some features of the chemistry and the stereochemistry are not revealed by the spectra, like the conformation of both cyclohexane and γ-lactone rings, the equatorial conformation of the secondary hydroxyl group, the stereochemistry of the methyl group attached at C(11), the vinyl group attached at C(10) and the substituent attached at C(5). In order to establish a definitive structure, an X-ray analysis of the elemanolide single-crystal was carried out

Table 1 Atomic co-ordinates ($\times 10^4$) of melitensin

Atom	*X*	*Y*	*Z*
C(1)	8180 (9)	5754 (7)	7524 (4)
C(2)	9562 (12)	5563 (11)	7909 (5)
C(3)	6990 (10)	2150 (7)	7523 (4)
C(4)	6428 (8)	3299 (6)	7672 (4)
C(5)	6110 (8)	4278 (6)	7017 (4)
C(6)	5415 (8)	3771 (6)	6234 (4)
C(7)	4841 (8)	4835 (6)	5684 (4)
C(8)	6275 (9)	5544 (6)	5379 (4)
C(9)	7152 (9)	6064 (7)	6125 (4)
C(10)	7632 (9)	5051 (7)	6771 (4)
C(11)	3774 (8)	4125 (7)	5088 (4)
C(12)	3068 (9)	3145 (7)	5689 (4)
C(13)	2446 (11)	4876 (8)	4675 (5)
C(14)	8957 (8)	4208 (8)	6408 (4)
C(15)	5977 (10)	3748 (7)	8528 (4)
O(1)	6238 (6)	2859 (5)	9147 (2)
O(2)	3977 (6)	3034 (4)	6347 (3)
O(3)	1923 (7)	2502 (6)	5556 (3)
O(4)	5818 (6)	6569 (4)	4861 (2)

RESULTS AND DISCUSSION

The title compound crystallizes in the orthorhombic space group $P2_12_12_1$ (No. 19), $a = 8.469(5)$, $b = 10.769(5)$, $c = 16.452(5)$ Å, $V = 1500.5$ Å^3, $D_H = 1.177$ Mgm^{-3}, $Z = 4$. The molecule projected along the [001] direction is shown in Fig. 1 and Table 1 gives the final atomic coordinates

The present study showed the presence of two fused rings, one a five-membered γ-lactone and another of six carbon atoms The γ-lactone carries a CO group at C(12), and α-oxygen between C(6) and C(12) and an equatorial methyl group at C(11). The six-membered ring has a chair conformation, with an equatorial hydroxyl group at C(8), an equatorial vinyl at C(10), an axial methyl at C(10) and an equatorial CH_2=CH(CH_2OH) group at C(5) Both rings are *trans*-fused by equatorial bonds. Therefore in

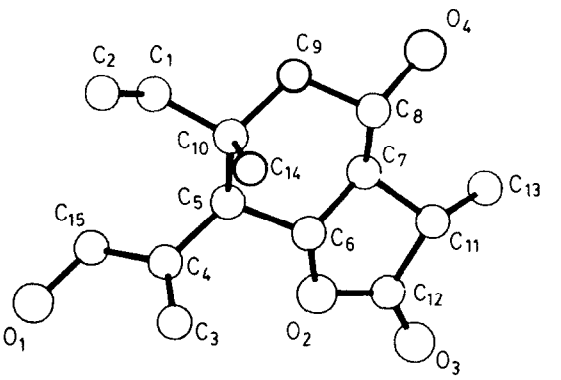

Fig. 1.

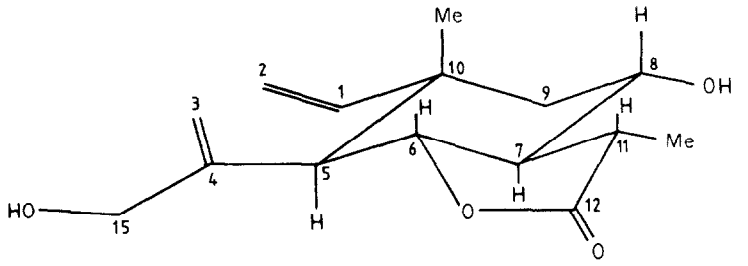

Fig 2

agreement with the chemical studies of the preceding paper [3] and with the information gained by the X-ray study the compound is 8α,15-dihydroxyelema-1,3 dien-6α,12-olide

The crystal structure is built by one intermolecular hydrogen bond between O(1)–H O(4) with O(4) . . O(1)=2.824(7) Å The existence of this hydrogen bonding between two O(1) and two O(4) from four different molecules can be seen from a packing diagram [4] The solid compound adopts a conformation with the double bond at C(1)–C(2) and the methyl group at C(10) synperiplanar {torsion angle C(2)–C(1)–C(10)–C(9) −128 1(7)°}, and with the double bond at C(3)–C(4) and the hydroxyl group at C(4) synperiplanar {torsion angle C(3)–C(4)–C(15)–O(1) 1.4(10)°}. There is interaction between C(14) and C(3) with a torsion angle C(3)–C(4)–C(5)–C(10) of −84 2(8) (Fig. 2) The α-methyl γ-lactone ring, *trans*-fused between C(6) and C(7), adopts a flattened envelope conformation, here C(7) is displaced by 0 60 Å from the plane defined by O(2)–C(16)–C(11)–C(12)

EXPERIMENTAL

For the X-ray structure analysis the data collection was performed with the aid of a Enraf-Nonius CAD-4 diffractometer The cell dimensions were obtained by least squares from the setting angles of 25 reflections With MoKα radiation (graphite monochromator) 1529 independent reflections were measured in the ω-2θ scan mode, of which 1493 reflections with $I \geq 1\ 5\sigma(I)$ were considered as observed and included in the refinement Corrections were made for the Lorentz and polarization effects, but not for absorption

The structure was solved by direct methods using the MULTAN 80 computer system [5] Full-matrix least-squares refinement with the program CRYLSQ (X-Ray System 70) [6] was completed with anisotropic thermal parameters for non-hydrogen atoms The H atoms were not taken into account in this work The final R was 0 081

The lists of structure factors and anisotropic thermal parameters of non-hydrogen atoms have been deposited in the Cambridge Crystallographic Data Centre

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