Phytochemistry, Vol 23, No 9, pp 1999–2001, 1984
Printed in Great Britain

0031–9422/84 \$3 00+0 00

STRUCTURE AND STEREOCHEMISTRY OF STENOPHYLLOLIDE, A GERMACROLIDE FROM *CENTAUREA ASPERA* VAR. *STENOPHYLLA*

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(*Revised received* 24 *January* 1984)

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

Abstract—A crystalline compound, named stenophyllolide, obtained from an extract of *Centaurea aspera* var *stenophylla* was shown to be 9β,15-dihydroxygermacra-1(10),4,11-trien-6α,12-olide by X-ray analysis The molecular structure of stenophyllolide was solved with orthorhombic space group $P2_12_12_1$, $a = 11\,719$ (5), $b = 13\,389$ (5), $c = 8\,646$ (5) Å for $Z = 4$, by direct methods and refined to a final R of 0 06 for 1198 observed reflections

INTRODUCTION

Stenophyllolide is a crystalline compound isolated by Sánchez Parareda *et al* [1] some time ago, and recently by Picher *et al* [2] from *Centaurea aspera* L ssp *stenophylla* (Dufour) Nyman Although the ^{1}H NMR spectra favour the structure of 9,15-dihydroxygermacra-1(10),4,11-trien-6,12-olide, other structures could not be definitively eliminated and some features of the chemistry and the stereochemistry are not shown by the spectra, like the conformation of both cyclodecadien and γ-lactone rings, the *trans*-nature of two double bonds and the equatorial conformation of the secondary hydroxyl group In order to establish definitively all these features an X-ray analysis of the stenophyllolide single-crystal was carried out The molecular structure of this compound has not yet been reported in the literature [3]

RESULTS AND DISCUSSION

The title compound crystallizes in the orthorhombic space group $P2_12_12_1$ (No 19), $a = 11\,719$ (5), $b = 13\,389$ (5), $c = 8\,646$ (5) Å, $V = 1357$ Å^3, $D_x = 1\,298$ Mg m^{-3}, $Z = 4$

Figure 1 shows the molecule projected along the |001| direction Table 1 gives the final atomic coordinates while intramolecular distances and angles for the non-hydrogen atoms are shown in Tables 2 and 3, and some important torsion angles are given in Table 4

The present study showed the presence of two fused rings, one a five membered γ-lactone and another of ten carbon atoms with two double bonds The γ-lactone carries a CO group at C(12), and α-oxygen between C(6) and C(12) and an exocyclic double bond at C(11)–C(13) [1 318 (9) Å] Double bonds of the cyclodecadien ring, placed at C(4)–C(5) [1 353 (8) Å] and C(1)–C(10) [1 318 (9) Å] are *trans* and therefore the compound belongs to the class of germacrolides [4] There is an equatorial hydroxyl group at C(9), a methyl at C(10) and a CH_2OH group at C(4) Both rings are *trans*-fused by equatorial bonds Therefore in agreement with the chemical studies of the preceding paper, and with the information gained by this X-ray study the compound should be represented as 9β,15-dihydroxygermacra-1(10),4,11-trien-6α,12-olide

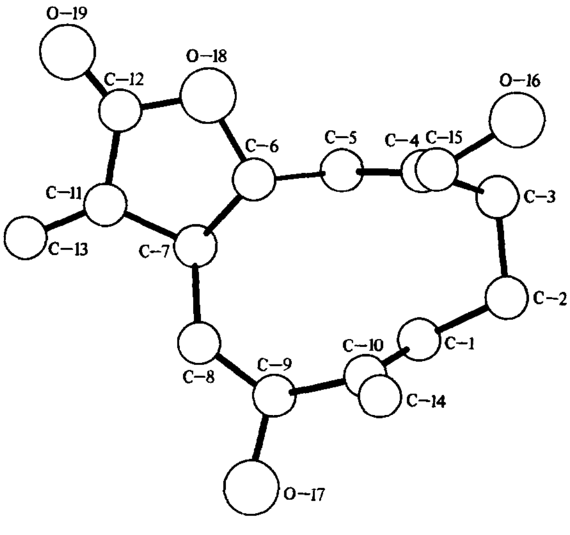

Fig 1

In addition there is one intermolecular hydrogen bond between O(16) and O(17) [2 734 (6) Å], and the solid compound adopts a conformation of a cross-structure for the decadien-ring with the groups Me and CH_2OH situated parallel in the same side [5] in accord with Fig 2

The valency angles of the cyclodecadiene ring range from 107 0 (5)° to 127 8 (6)°, mean 116 4 (5)°, and the large deviations from the tetrahedral value indicate a considerable amount of angular strain The mean valency angle commonly found in the cyclodecadiene ring is 113 5° [6], and the difference of 2 5° indicates a small strain due to the substitutes in the ring

Table 1. Atomic coordinates ($\times 10^4$)

	x	*y*	*z*
C(1)	197 (5)	2241 (4)	8608 (8)
C(2)	−1030 (5)	2538 (4)	8281 (9)
C(3)	−1152 (6)	3712 (4)	8427 (8)
C(4)	−298 (5)	4163 (4)	7365 (8)
C(5)	760 (5)	4327 (4)	7938 (7)
C(6)	1847 (5)	4412 (4)	7067 (8)
C(7)	2806 (5)	3774 (4)	7772 (7)
C(8)	2957 (5)	2691 (4)	7164 (7)
C(9)	2191 (5)	1909 (5)	7976 (7)
C(10)	942 (5)	1970(4)	7546 (7)
C(11)	3841 (5)	4433 (4)	7514 (7)
C(12)	3412 (6)	5463 (4)	7303 (9)
C(13)	4938 (6)	4218 (5)	7473 (9)
C(14)	691 (5)	1778 (5)	5878 (8)
C(15)	−560 (5)	4196 (5)	5697 (8)
O(16)	−1686 (3)	4586 (3)	5486 (5)
O(17)	2677 (3)	949 (3)	7580 (5)
O(18)	2271 (4)	5452 (3)	7165 (6)
O(19)	3939 (4)	6237 (3)	7269 (7)

Table 2. Intramolecular distance (Å)

C(1)–C(2)	1.519 (9)	C(4)–C(15)	1.475 (9)
C(2)–C(3)	1.583 (8)	C(15)–O(16)	1.431 (8)
C(3)–C(4)	1.486 (9)	C(9)–O(17)	1.447 (6)
C(4)–C(5)	1.353 (8)	C(10)–C(14)	1.494 (9)
C(5)–C(6)	1.484 (9)		
C(6)–C(7)	1.538 (8)	C(7)–C(11)	1.516 (8)
C(7)–C(8)	1.552 (7)	C(11)–C(12)	1.478 (8)
C(8)–C(9)	1.547 (8)	C(12)–O(18)	1.343 (8)
C(9)–C(10)	1.512 (8)	O(18)–C(6)	1.481 (7)
C(10)–C(1)	1.318 (9)	C(11)–C(13)	1 318 (9)
		C(12)–O(19)	1 207 (8)

Table 3. Intramolecular angles (°)

C(1)–C(2)–C(3)	109.3 (5)	C(9)–C(10)–C(14)	114.8 (5)
C(2)–C(3)–C(4)	107.0 (5)	C(14)–C(10)–C(1)	126.1 (6)
C(3)–C(4)–C(5)	117.2 (6)		
C(4)–C(5)–C(6)	127.8 (6)	C(5)–C(6)–O(18)	109.3 (5)
C(5)–C(6)–C(7)	112.5 (5)	C(8)–C(7)–C(11)	113.8 (5)
C(6)–C(7)–C(8)	117.9 (5)		
C(7)–C(8)–C(9)	114.4 (5)	C(6)–C(7)–C(11)	101.7 (4)
C(8)–C(9)–C(10)	114.4 (5)	C(7)–C(11)–C(12)	106.8 (5)
C(9)–C(10)–C(1)	119 0 (5)	C(11)–C(12)–O(18)	109.8 (5)
C(10)–C(1)–C(2)	124 8 (6)	C(12)–O(18)–C(6)	110.4 (4)
C(3)–C(4)–C(15)	118.4 (5)	O(18)–C(6)–C(7)	104.7 (4)
C(15)–C(4)–C(5)	122.9 (6)	C(7)–C(11)–C(13)	131 0 (5)
C(4)–C(15)–O(16)	109.1 (5)	C(13)–C(11)–C(12)	122 1 (6)
C(8)–C(9)–O(17)	105.4 (4)	C(11)–C(12)–O(19)	129 1 (6)
O(17)–C(9)–C(10)	111.7(4)	O(19)–C(12)–O(18)	121 1 (6)

Table 4. Torsion angles (°)

C(1)–C(2)–C(3)–C(4)	45.6 (6)
C(2)–C(3)–C(4)–C(5)	−79.8 (6)
C(3)–C(4)–C(5)–C(6)	153.6 (5)
C(4)–C(5)–C(6)–C(7)	−132.1 (5)
C(5)–C(6)–C(7)–C(8)	91.3 (5)
C(6)–C(7)–C(8)–C(9)	−85.6 (5)
C(7)–C(8)–C(9)–C(10)	72.6 (5)
C(8)–C(9)–C(10)–C(1)	−113.2 (5)
C(9)–C(10)–C(1)–C(2)	166.9 (5)
C(10)–C(1)–C(2)–C(3)	−98.4 (6)
C(6)–C(7)–C(11)–C(12)	21.2 (5)
C(7)–C(11)–C(12)–O(18)	−9.6 (6)
C(11)–C(12)–O(18)–C(6)	−7 3 (5)
C(12)–O(18)–C(6)–C(7)	21.0 (6)
O(18)–C(6)–C(7)–C(11)	−24 9 (5)

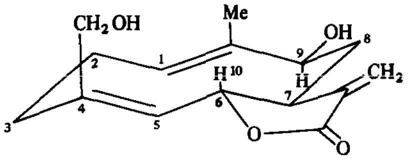

Fig. 2.

The α-methylene γ-lactone ring, *trans*-fused between C(6) and C(7), adopts a flatted envelope conformation; here C(7) is displaced by 0.60 Å from the plane defined by O(16)–C(6)–C(11)–C(12); the torsion angles C(5)–C(6)–C(7)–C(8) [91.3 (5)°] and O(18)–C(6)–C(7)–C(11) [−24.9 (5)°] are usually found in *trans*, *trans*-germacranolides [7].

The Cotton effect at 260 nm for the α-methylene γ-lactone Chromophore *n* → π* transition state is a negative one in accord with the Stöckling rule [8] which relates the negative Cotton effect with the *trans*-fusion of the γ-lactone ring. This rule seems to have no exceptions for the *trans*, *trans*-germacranolides; the exceptions mentioned in the literature are given by helangolides, in which the *cis*-C(4)–C(5) double bond changes the torsion angles and the chirality of the chromophore [7]. CD (*c* 0.5 mg/ml, MeOH) Δ_{260} − 1.86.

EXPERIMENTAL

For the X-ray structure analysis the data collection was performed with the aid of a Philips PW 1100 four-circle diffractometer. The cell dimensions were obtained by least squares from the setting angles of 25-reflections. With MoKα radiation (graphite monochromator) 1389 independent reflections were measured in the ω-2θ scan mode, of which 1198 reflections with $I \geqslant 1.5\sigma(I)$ 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 Random-Phase Approach of Debaerdemaeker and Woolfson [9] The computation of an E map with the phases of the set with the highest 'combined figure of merit' revealed the position of the C atom of the ten-membered and γ-lactone rings. The remaining atoms of the molecule were found by successive refinements and Fourier synthesis. Full-matrix least-squares refinement with the program SHELX 77 [10] was completed with anisotropic thermal parameters for non-hydrogen atoms. The H atoms were included at the final stage of the refinement in calculated positions with an overall isotropic temperature factor The final R was 0 0654

The list of structure factors, positional and temperature factors of all atoms, intramolecular distances and angles have been deposited in the Cambridge Crystallographic Data Centre

Acknowledgements—We are indebted to the Spanish 'Comisión Científica Nacional' for financial support and to J De Pascual Teresa, Professor of Organic Chemistry of the University of Salamanca for running the CD curve One of us (T D) wishes to thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for supporting this work

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