Chemistry of Natural Compounds, Vol. 32, No. 2, 1996

CRYSTAL AND MOLECULAR STRUCTURE OF THE GUAIANOLIDE GAILLARDIN

K. A. Éshbakova, M. K. Makhmudov, G. V. Sagitdinova,
and B. Tashkhodzhaev

UDC 547.992:547.37+548.737

The epigeal part of Pulicaria uliginosa (P. dysenterica) *has been investigated for the first time for its γ-lactone content. The guaiane γ-lactone gaillardin,* $C_{17}H_{22}O_5$ *has been isolated, and its crystal and molecular structures have been established by the x-ray structural method (diffractometer,* CuK_α*, 770 reflections, direct method,* $R = 0.108$*).*

Continuing an investigation of an extract of the epigeal part of fleabane mullet *Pulicaria uliginosa* [1], we have isolated from the chloroform extract a crystalline substance $C_{17}H_{22}O_5$, mp 188-190°C $[\alpha]_D$ ±0°(*c* 0.5, chloroform).

According to its IR spectrum (3520, 1770, 1735, 1680 cm^{-1}) the substance was an acylated γ-lactone. It contained acetyl and hydroxy groups, as was confirmed by mass spectroscopy and PMR.

The mass spectrum showed peaks of ions with *m/z* 306 (M^+), 288 ($M^+ - H_2O$) and 247 ($M^+ - OCOCH_3$).

The substance was not acetylated by acetic anhydride in pyridine with heating, which showed the tertiary character of its hydroxy group.

In the PMR spectrum we observed the signals of a methyl at a double bond (s, 1.75 ppm, 3H), a methyl at a heteroatom (s, 1.18 ppm, 3H), the methyl of an acetyl group (s, 2.00 ppm, 3H), a lactone proton (br.d., J = 10 Hz, 4.4 ppm, 1H), the protons of an exomethylene group (two doublets at 5.47 and 6.12 ppm, s, with J = 3.5 Hz, 1H each), and two 1H signals in the form of highly broadened singlets at 5.24 and 5.8 ppm which could be assigned to geminal and olefinic protons.

The combination of spectral results permitted the suggestion of a number of alternative structures for the γ-lactone. In order to determine the structure reliably, we carried out an x-ray structural analysis (XSA) of a crystal of the γ-lactone under consideration, since we had available only a few crystals of the substance. According to the XSA results, it was identical with gaillardin (**1**), isolated previously from *Gaillarda pulchella* [2], *Inula oculus christi* [3], *Inula britannica* L.s.I. [4], and *Inula britannica* L. var. *chinensis* (Rupr.) Regel [5]. This is the first time that the plant *Pulicaria uliginosa* has been investigated for the presence of lactones.

The general shape of the (**1**) molecule is shown in Fig. 1. Bond lengths and valence angles are given in Table 1. Within the limits of experimental error, their values agree with the corresponding standard magnitudes [6] and those observed for other natural gaillardin derivatives [7]. It can be seen from Fig. 1 that the hydroxy groups at C1 and C4 are α-orientated and that the lactone ring is condensed at C7-C8. According to the torsional angles H1C1C5H5 (−171.3°) and H7C7C8H8 (155.4°), rings *A/B* and *B/C* are *trans*-linked.

In the (**1**) molecule the five-membered ring *A* has a 1α,2β-half-chair conformation and the lactone ring is present in the form of an 8α-envelope. The seven-membered ring *B*, containing a double bond in the C9=C10 position, is slightly distorted in comparison with the canonical form — a 6β,9,10α-chair: the four atoms C1, C5, C7, and C8 are in one plane with an accuracy of ±0.07 Å. It must be mentioned that in another natural gaillardin derivative — deacetyldihydrogaillardin *p*-bromobenzoate [7] — rings *A* and *C* have the forms of a 2α-envelope and a 7β-envelope, respectively, while ring *B* is an ideal 6α,9,10β-chair. Such a difference in the conformations of rings *A* and *C* is apparently connected with the presence of different substituents at C2 and C11, respectively.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Republic of Uzbekistan, Tashkent, fax (3712) 89 14 75. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 202-205, March-April, 1996. Original article submitted November 20, 1995.

0009-3130/96/3202-0180$15.00

TABLE 1. Bond Lengths r (Å) and Valence Angles ω (degrees) in the (**1**) Molecule

Bond	r	Angle	ω	Angle	ω
C1-C2	1.55(2)	C2-C1-C5	101.8(13)	C8-C7-C11	102.0(12)
C1-C5	1.57(2)	C2-C1-C10	114.3(13)	C7-C8-C9	116.1(13)
C1-C10	1.51(3)	C5-C1-C10	121.0(14)	C7-C8-O1	103.6(12)
C2-C3	1.50(3)	C1-C2-C3	102.8(14)	C9-C8-O1	111.3(13)
C2-O3	1.47(2)	C1-C2-O3	105.4(13)	C8-C9-C10	124.9(16)
C3-C4	1.53(3)	C3-C2-O3	110.4(14)	C1-C10-C9	118.6(15)
C4-C5	1.54(2)	C2-C3-C4	104.3(16)	C1-C10-C15	122.3(14)
C4-C14	1.51(3)	C3-C4-C5	108.2(15)	C9-C10-C15	118.1(17)
C4-O5	1.43(2)	C3-C4-C14	111.7(16)	C7-C11-C12	107.4(14)
C5-C6	1.53(2)	C5-C4-C14	114.1(14)	C7-C11-C13	127.8(15)
C6-C7	1.57(2)	C3-C4-O5	109.3(14)	C12-C11-C13	124.4(15)
C7-C8	1.54(2)	C5-C4-O5	106.8(14)	C11-C12-O1	109.3(14)
C7-C11	1.51(2)	C14-C4-O5	106.6(15)	C11-C12-O2	130.1(16)
C8-C9	1.48(2)	C1-C5-C4	102.8(12)	O1-C12-O2	120.6(15)
C8-O1	1.48(2)	C1-C5-C6	120.4(12)	C17-C16-O3	105.5(15)
C9-C10	1.33(2)	C4-C5-C6	115.4(14)	C17-C16-O4	130.0(16)
C10-C15	1.46(3)	C5-C6-C7	110.6(13)	O3-C16-O4	124.5(19)
C11-C12	1.45(2)	C6-C7-C8	111.9(13)	C8-O1-C12	109.9(13)
C11-C13	1.35(3)	C6-C7-C11	115.2(14)	C2-O3-C16	116.0(15)
C12-O1	1.38(2)				
C12-O2	1.22(2)				
C16-C17	1.50(3)				
C16-O3	1.38(2)				
C16-O4	1.15(3)				

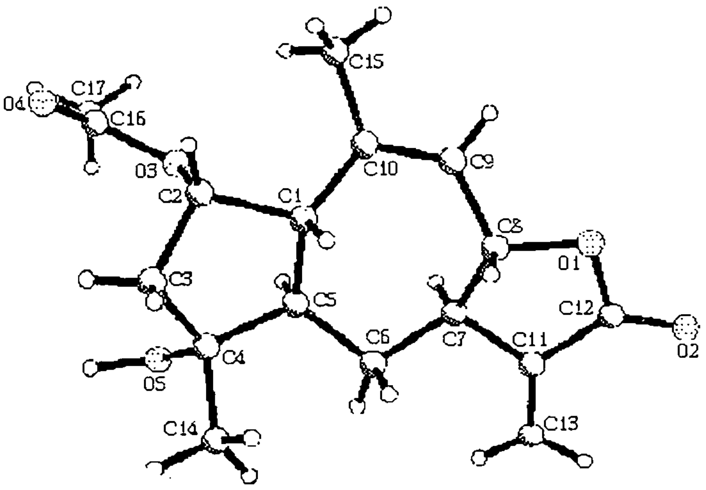

Fig. 1. Structure of the gaillardin molecule.

Packing of the Molecules. Analysis of the crystal structure of (1) showed the presence of intermolecular H-bonds of the O-H···O type. The acetyl group at C1 of the initial molecule is close to the C-4 OH group of another molecule transformed by 2_1 screw symmetry along the *a* crystallographic axis (O4···O5 distance 2.87 Å)

EXPERIMENTAL

The conditions for recording the spectra have been given in [8]. For TLC we used Silufol (Chemapol) and the solvent systems: 1) hexane–ethyl acetate (3:1); 2) chloroform–ethyl acetate (4:1). The revealing agent — a 5% solution of vanillin in concentrated sulfuric acid — gave a claret coloration.

Isolation of Gaillardin. The comminuted air-dry epigeal part of the plant (1.5 kg) was extracted four times with chloroform, and the chlorophylls were precipitated by the usual method. After elimination of the solvent the material obtained was chromatograped on a column with neutral alumina (activity grade IV) as sorbent and was eluted with hexane–ethyl acetate

TABLE 2. Coordinates ($\times 10^4$) and Temperature Factors (Å^2 $\times$ 10^3) of the Nonhydrogen Atoms of the (**1**) Molecule

Atom	x	y	z	U_{eq}
C1	445(33)	8794(19)	1201(4)	44(6)
C2	442(28)	8540(25)	739(5)	55(7)
C3	1452(34)	6859(29)	693(5)	72(8)
C4	3290(31)	6789(23)	1016(5)	55(6)
C5	2863(25)	8190(22)	1318(4)	42(6)
C6	3438(31)	7799(18)	1755(4)	42(5)
C7	2906(27)	9309(23)	2032(4)	47(6)
C8	358(28)	9684(21)	2049(4)	42(6)
C9	−523(31)	10770(22)	1728(5)	55(7)
C10	−405(31)	10455(25)	1335(4)	55(7)
C11	3471(31)	9076(19)	2472(5)	44(6)
C12	1755(30)	9929(20)	2704(5)	47(6)
C13	5344(35)	8404(22)	2630(4)	58(7)
C14	3443(37)	5106(21)	1206(5)	71(8)
C15	−1491(41)	11608(26)	1058(6)	90(9)
C16	1980(43)	9994(23)	167(5)	65(8)
C17	3849(32)	11189(27)	79(5)	72(8)
O1	48(23)	10429(15)	2451(3)	55(4)
O2	1679(23)	10240(15)	3062(3)	66(5)
O3	1979(19)	9802(16)	579(3)	52(4)
O4	756(25)	9337(21)	−49(3)	95(7)
O5	5424(20)	7104(18)	836(3)	74(5)

mixtures having successively increasing concentrations of the latter. The solvent with a ratio of 6:1 eluted gaillardin, $C_{17}H_{22}O_5$, mp 188-190°C, yield 0.001% of the weight of the raw material, R_f 0.4 (systems 1 and 2). UV spectrum, λ_{max} 220 nm.

X-Ray Structural Analysis. Crystals grown from solution in aqueous ethanol were first treated by the photo method. The unit cell parameters and the space group were determined and refined on a Syntax P-2_1 diffractometer: a = 5.940(1), b = 8.118(2), c = 33.230(7) Å, d_{calc} = 1.270 g/cm^3, space group $P2_12_12_1$, Z = 4.

A three-dimensional set of intensities was obtained on the same diffractometer by the $\theta/2\theta$ method of scanning using CuK_α radiation (graphite monochromator), sin $\theta/\lambda < 0.31$, rate of scanning 10 deg/min, number of independent nonzero reflections with $I > 2\sigma(I)$ 770. The absence of a good statistical set is connected with the limited choice of crystals suitable for XSA.

The structure was determined by the direct method using the SHELX-86 program [9] (PC DOS version), where, in the automatic regime, we succeeded in finding a model of the molecule, and it was refined by the method of least squares (MLS) successively in the isotropic-anisotropic approximation by the SHELX-76 program [10]. The coordinates of H atoms linked to carbon atoms were calculated geometrically, and those of OH groups were found from a difference electron density synthesis and were refined isotropically. The final value of the divergence factor R = 0.108 (R_w = 0.109). The coordinates of the nonhydrogen atoms from the last stage of the MLS are given in Table 2.

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