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STRUCTURE OF SUBCHRYSIN

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A new sesquiterpene lactone having the structure 3β-acetoxy-1β-hydroxy-6β,7α(H)-germacra-4,10(14),11(13)-trien-6,12-olide has been isolated from Artemisia subchrysolepis *Filat. and has been called subchrysin. Its stereochemistry has been established by x-ray structural analysis.*

Artemisia subchrysolepis Filat. has recently been described as an individual species by N. S. Filatova and, according to the systematics of higher plants, is included in the subgenus *Seriphidium* (Bess.) Peterm., section *Sclerophyllum* Filat., subsection *Kazakhstaniceae* Filat. [1].

We have made a phytochemical study of this plant. From its epigeal part we have isolated: β-sitosterol, α-santonin, and a new sesquiterpene lactone, which has been called subchrysin (1). Lactone (1) has the composition $C_{17}H_{22}O_5$, but in its mass spectrum a peak was observed at *m/z* 264, corresponding to a $C_{15}H_{20}O_4$ ion formed by the splitting out of ketene from the molecular ion [2]. An analogous fragmentation that is characteristic for a number of sesquiterpene lactone acetates has been described previously [3].

The molecule of subchrysin (1) has one secondary OH group, the acetylation of which led to compound (2), described as ridentin diacetate and identified by comparing its ^1H NMR spectrum with that given in the literature [4].

Table 1 gives details of the ^1H NMR spectra of compounds (1) and (2). We may note that the signals of some protons in the ^1H and ^{13}C NMR spectra of subchrysin (1) are broadened because of conformational exchange at room temperature, although the broadening of the H-1, H-3, and H-5 signals in the (1) molecule practically disappeared on heating to 90°C.

In order to establish the spatial structure of subchrysin, we performed an x-ray structural investigation of it. The general shape of the (1) molecule is shown in Fig. 1. The bond lengths and valence angles differ insignificantly from the ideal values for sp^3- and sp^2-hybridized atoms [5]. The ten-membered and the lactone rings are linked in the *trans*- manner (the H6C6C7H7 torsional angle is −161.3°). The hydroxy group at the C1 atom and the acetoxy group at the C3 atom have the β-orientation. The C2C1C10C9 and C3C4C5C6 torsional angles are −54.4° and 155.4°, respectively, because of which compound (1) may be assigned to the type of Z,E-germacranolides.

The methylene group at the C10 atom and the methyl group at the C4 atom are anti-oriented, in the α- and β-directions, respectively, which permits the conformation of the ten-membered ring in compound (1) to be characterized as of the $^{15}D_5,{}_1D_{14}$ chair−boat type (the torsional angles are given in Table 2).

The conformation of the lactone ring in (1) is a 6β,7α-half-chair ($\Delta C_2^{12} = 3.3°$).

Thus, compound (1) is 3β-acetoxy-1β-hydroxy-6β,7α(H)-germacra-4,10(14),11(13)-trien-6,12-olide.

EXPERIMENTAL

IR spectra were obtained on a UR-20 instrument; ^1H and ^{13}C NMR spectra on Bruker DRX-500 and Bruker WP-400SY instruments, and mass spectra (EI, 70 eV) on a Finnigan MAT 8200 instrument. Melting points were determined on a Kofler stage. Optical rotations were measured for solutions in $CHCl_3$ on a Polamat A polarimeter (at 580 nm).

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TABLE 1. Details of the ^{1}H NMR Spectra of Compounds (1) and (2) (δ, 400 MHz, J, Hz, CDCl$_3$)

Compound	H-1	H-3	H-5	H-6	H-13 H-13''	H-14 H-14''	H-15	OAc
1*	4.28dd (10.0;4.0)	5.43dd (10.0;4.5)	5.56br.d (10)	4.54 td (10;1.2)	6.22dd (3.5;1.0) 5.42dd (3.5;1.0)	5.31br.s 4.96 br.s	1.77dd (3H,1.4;0.6)	2.03c (3H,s)
1	4.09 (1H, m)	5.18 (1H,br.d, 10)	5.39 (1H,d,10)	4.41 (1H, tr,10)	5.44 (1H d,3.4) 6.17 (1H,d,3.4)	4.92 (1H, br.s) 5.24 (1H, br.s)	1.72 (3H, br.s :)	2.04 (3H,s
2*	5.08 (1H,m)	5.23 (1H,dd,10,3.5)	5.49 (1H,d,10)	4.37 (1H tr, 10)	5.43 (1H d,3.0) 6.20 (1H,d,3.0)	5.02 (1H, br.s) 5.24 (1H,br.s :)	1.67 (3H,br.s)	1.97 (3H,s) 2.03 (3H,s)

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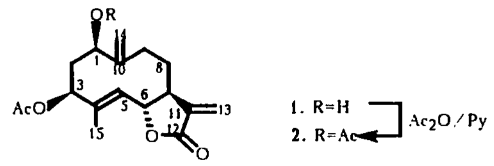
*500 MHz, Py-d$_5$, +90°C.

**200 MHz.



1. R=H

2. R=Ac

TABLE 2. Intracyclic Torsional Angles φ (degrees) of Molecule (1)

Angle	φ	Angle	φ
C1C2C3C4	88.6	C9C10C1C2	-54.4
C2C3C4C5	-105.6	C10C1C2C3	-57.9
C3C4C5C6	155.4	C6C12C12C1	-13.2
C4C5C6C7	-119.0	C1C12C11C7	-10.0
C5C6C7C8	84.2	C12C11C7C6	26.6
C6C7C8C9	-56.2	C11C7C6O1	-33.4
C7C8C9C10	-51.3	C7C6O1C12	30.1
C8C9C10C1	165.0		

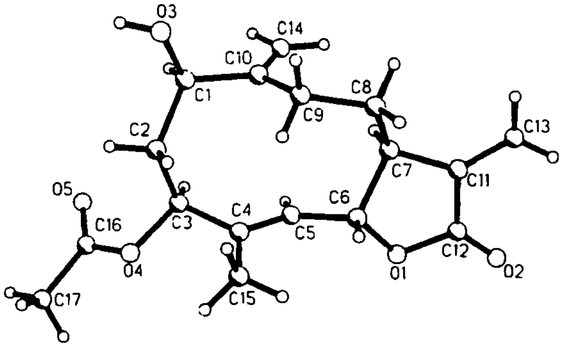


Fig. 1. Structure of the subchrysin molecule.

Procedure for Isolating (1). The epigeal part of *Artemisia subchrysolepis* (1 kg) gathered in 1994 in the flowering phase (July) in the environs of the village of Urdzhar, Semipalatinskaya oblast, was extracted with chloroform (3 × 3 liters) at the boil in a flask with a reflux condenser. The combined extracts were evaporated in a rotary evaporator. This gave a total of 133 g of extractive substances, which was treated with a mixture of alcohol and water (0.2 liter of EtOH and 1 liter of H_2O). The resulting precipitate of ballast substances was filtered off, treated twice with a mixture of alcohol and water (0.3 liter of EtOH and 1 liter of H_2O) at t = 70°C, and filtered off again. The combined aqueous alcoholic extract was treated with $CHCl_3$ (3 × 0.2 liter). The chloroform layers were combined and evaporated to a dry residue (63 g), which was deposited on a column containing 0.7 kg of type KSK silica gel. Elution with benzene and mixtures of benzene with EtOAc yielded successively fractions containing β-sitosterol (0.05 g) and α-santonin (0.51 g), and subchrysin (1) (3.44 g). Repeated flash chromatography (with eluents containing from 0 to 60% of EtOAc) led to the isolation of 300 mg of lactone (1).

3β-Acetoxy-1β-hydroxy-6β,7α(H)-germacra-4,10(14),11(13)-trien-6,12-olide (1). mp 149-151°C (EtOAc), $[\alpha]^{21}_{580}+145.4°$ (*c* 0.44; $CHCl_3$).

IR spectrum (ν, cm^{-1}, KBr): 3470 (OH), 3075, 900 ($C=CH_2$), 1760 (γ-lactone), 1715, 1260 (OAc), 1660, 1450 (−HCCH−), 975 (−HCCH−, *trans*).

Mass spectrum (*m/z*, I, %): 264 $[M\text{-}O]^+$ (8.16), 246 $[M-CH_2\text{-}C=O\text{-}H_2O]^+$ (12.80), 228 $[M-CH_2=C=O\text{-}2H_2O]^+$ (8.49), 203 (10.69), 191 (20.40), 178 (7.36), 175 (10.95), 149 (19.93), 131 (11.71), 121 (17.87), 119 (15.01), 105 (18.59), 95 (22.65), 91 (25.33), 81 (18.92), 79 (20.95), 67 (13.65), 55 (20.33), 53 (22.92), 43 (100.0), 41 (25.61), 28 (34.23). Found (*m/z*): 264.13794 $[M\text{-ketene}]^+$. Calculated for $C_{15}H_{20}O_4$: 264.13615.

^{13}C NMR (125 MHz, Py−D_5, +90°C): 11.94 q (C-15), 20.34 q (C-17), 26.24 t (c-8), 30.39 t (C-9), 38.81 t (C-2), 47.74 d (C-7), 74.87 d (C-1), 76.53 d (C-3), 79.52 d (C-6), 111.06 t (C-14), 117.44 t (C-13), 124.47 d (C-5), 140.80 s (C-11), 142.50 s (C-4), 150.66 s (C-10), 169.15 s (C-12), 169.51 s (C-16).

Elementary Analysis. Found, %: C 66.40; H 7.20. Calculation, %: C 66.65; H 7.24.

1,3β-Diacetoxy-6β,7α(H)-germacra-4,10(14),11(13)-trien-6,12-olide (2). mp 65-68°C (ethyl acetate) $[\alpha]^{21}_{580}+200°$ (*c* 1.67; $CHCl_3$).

IR spectrum (ν, cm^{-1}, CCl_4): 3080 ($C=CH_2$), 1780 (γ-lactone), 1740, 1250 (OAc), 1665, 1440, 975 (−HC=CH−, *trans*), 910 ($C=CH_2$).

For the ^1H NMR spectrum, see Table 1.

TABLE 3. Coordinates of the Nonhydrogen Atoms in Structure of (**1**) ($\times 10^4$)

Atom	x	y	z
O1	12809 (3)	-714	2651 (2)
O2	14839 (3)	-2098 (7)	2034 (3)
O3	7922 (3)	7265 (7)	1647 (3)
O4	7562 (2)	2530 (8)	4341 (2)
O5	5331 (3)	1952 (9)	3592 (2)
C1	8036 (4)	5201 (8)	1835 (3)
C2	8002 (4)	4855 (8)	2989 (3)
C3	8226 (3)	2728 (8)	3356 (2)
C4	9865 (3)	2258 (8)	3497 (2)
C5	10485 (3)	1165 (8)	2793 (3)
C6	12107 (3)	1236 (8)	2587 (3)
C7	12373 (3)	1927 (8)	1505 (3)
C8	12314 (4)	4126 (8)	1333 (3)
C9	10941 (3)	5205 (7)	1697 (3)
C10	9410 (4)	4502 (8)	1297 (3)
C11	13852 (3)	946 (8)	1334 (3)
C12	13957 (4)	-762 (9)	2019 (3)
C13	14929 (5)	1396 (10)	713 (4)
C14	9201 (5)	3469 (9)	462 (3)
C15	10731 (4)	3245 (9)	4366 (3)
C16	6120 (4)	2085 (9)	4346 (3)
C17	5604 (5)	1843 (11)	5399 (3)

X-Ray Structural investigation of (1). The cell parameters and the intensities of 2239 independent reflections were measured on a Syntex $P2_1$ diffractometer with monochromatized $Mo-K_\alpha$ radiation, $\theta/2\theta$ scanning, $2\theta \leq 56°$. Crystals monoclinic, $a = 8.905$ (3), $b = 6.831$ (3), $c = 13.217$ (5) Å, $V = 801.9$ (0.9) Å^3, $d_{calc} = 1.269$ g/cm^3, $z = 2(C_{17}H_{22}O_5)$, sp.gr. $P2_1P2_1P2_1$.

In the calculations we used 1464 reflections with $I > 3\sigma$. The structure was interpreted by the direct method and was refined by full-matrix MLS in the anisotropic approximation for the nonhydrogen atoms. The H atoms were given geometrically. The final residuals were $R = 0.056$ and $R_w = 0.058$. The coordinates of the nonhydrogen atoms are given in Table 3. All the calculations were made by means of the SHELXTL program package (PC Version) on an IBM PC/AT.

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