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# ARTEFIN — A NEW SESQUITERPENE LACTONE FROM *Artemesia filatovii*

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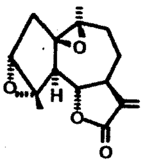
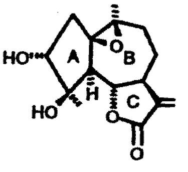
*Two sesquiterpene lactones of the guaiane type have been isolatd from the epigeal part of Artemisia filatovii; one has been identified as isoepoxyestafiatin, while the other has proved to be new and has been named artefin. The structure of artefin has been established on the basis of spectral (IR, PMR) characteristics and x-ray structural analysis.*

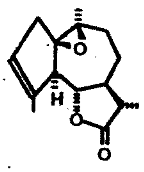
*Artemisia filatovii* is an endemic plant of Kazakhstan that was first found in Pavlodar province and described by A. N. Kupriyanov. We have studied the composition of the sesquiterpene lactones of this species of wormwood gathered in the environs of Ékibastuz, Pavlodar province. Two sesquiterpene lactones were isolated, one of which was identified from its physicochemical constants and spectral (IR, PMR) characteristics as isoepoxyestafiatin (**1**) [1], while the other proved to be new and has been named artefin (**2**).



**1**



**2**



**3**

Substance (**1**) — $C_{15}H_{18}O_4$, mp 167-170°C (ethyl acetate). Its IR spectrum contained absorption bands in the regions of 1760 cm$^{-1}$ (γ-lactone carbonyl conjugated with an exomethylene group) and 1660 cm$^{-1}$ (C=C).

Substance (**2**) — $C_{15}H_{20}O_5$, mp 206-208°C (ethyl acetate). Its IR spectrum contained absorption bands in the regions of (cm$^{-1}$) 3475, 3350 (OH group), 1750 (γ-lactone carbonyl conjugated with an exomethylene group), 1660 (C=C), and 1160 cm$^{-1}$ epoxy group).

The structure of the artefin molecule is shown in Fig. 1. The bond lengths in the molecule are the usual ones [2]. The five-membered rings are *trans*-linked with the seven-membered ring. Arborescin (**3**) is structurally very close to compound (**2**), which permits a geometric comparison to be performed. In the (**2**) molecule, ring *A* is in the form of an envelope (see Table 2) in which the C4 atom deviates (by 0.63 Å) in the direction of the OH group from the plane of the other atoms. In the arborescin (**3**) molecule, this ring has the same conformation, but the deviating atom is C10 (0.294 Å) [3]. The chair conformations of rings *B* in the (**2**) and (**3**) molecules practically coincide (the plane of symmetry passs through C7 and the center of the C1—C10 bond). In the (**2**) molecule, the lactone ring *C* has a *twist* form in which the C2 axis of symmetry passes through the C12 atom and the center of the C6—67 bond. In arborescin (**3**) the lactone ring has the form of a slightly distorted envelope with a deviation of the C7 atom by 0.595 Å. This conformational difference is obviously caused by hybridization of the C11 atom.

In the crystal, the molecules of (2) are bound by hydrogen bonds into two-dimensional paired networks parallel to the *ab* plane: O4-H...O2 (O4-H 0.92, H...O2 2.38, O4...O2 2.90 Å, O4-H...O2 116) and O5-H...O4 (05-H 1.17, H...O4 1.60, O5...O4 2.74 Å, O5-H...O4 161) (Fig. 2).

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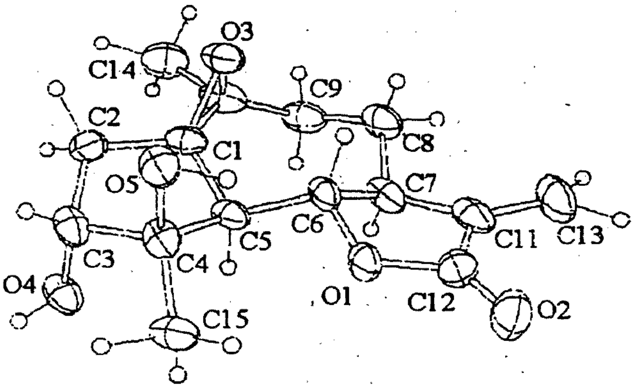

Fig. 1. The structure of the artefin molecule (**2**).

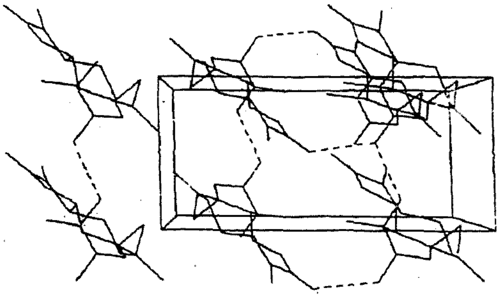

Fig. 2. Packing of the (**2**) molecules in the cell.

## EXPERIMENTAL

The individuality of the substances isolated was checked by TLC on Silufol plates in systems 1) ether, and 2) ethyl acetate. The revealing agent was 0.5% $KMnO_4$ in 0.5% $H_2SO_4$. For analysis, the substances were dried in a vacuum pistol with $P_2O_5$ (alcohol) for 6 h. Melting points were determined on a Boetius instrument.

PMR spectra were taken on a Bruker WP 200 SY instrument (200 MHz in deuterochloroform, 0 — TMS, $\delta$ scale). IR spectra (tablets with KBr) were recorded on a UR-20 spectrophotometer.

**Isolation of the Lactones.** The epigeal part of *Artemisia filatovii* was extracted five times with hot chloroform ($t$ = 60°C). After evaporation of the solvent, 87.8 g of a resin was obtained, and this was treated with 60% alcohol. The aqueous-alcoholic extract was treated with chloroform. After evaporation of the chloroform under vacuum, 14 g of total substances were obtained, and these were chromatographed on a column of KSK silica gel at a material—support ratio of 1:36. The column was eluted with benzene, benzene—ether (9:1 and 4:1), benzene—ethyl acetate (4:1), and ethyl acetate.

**Isolation of Isoepoxyestafiatin.** On elution of the column with benzene—ether (9:1), colorless crystals were isolated, and their recrystallization from ethyl acetate gave a colorless crystalline substance with the composition $C_{15}H_{18}O_4$, mp 167-170°C. IR spectrum ($cm^{-1}$): 2830, 2370, 1765, 1660, 1260, 1160, 1130, 1110, 960. PMR spectrum (multiplicity, ppm): 1.29 (3H, s); 1.65 (3H, s); 2.50 (1H, d, J = 11.5 Hz); 3.44 (1H, d, J = 3.5 Hz); 3.98 (1H, dd, J = 11.65 Hz, J = 10 Hz); 5.43 (1H, d, J = 3.5 Hz); 6.16 (1H, d, J = 3.2 Hz).

**Isolation of Artefin.** On further elution with benzene—ethyl acetate another crystalline substance was isolated. Recrystallization from ethyl acetate gave colorless acicular crystals with the composition $C_{15}H_{20}O_5$, mp 206-208°C. IR spectrum ($cm^{-1}$) 3475, 3350, 1750, 1660, 1320, 1250, 1185, 1160, 1120, 1055, 995, 950.

**The x-ray structural investigation of a single crystal of artefin (2)** was carried out on a SYNTEX-P2 diffractometer. The crystals of (**2**) were monoclinic: $a = 6.01(1)$, $b = 9.15(1)$, $c = 12.71(1)$ Å, $\beta = 91.66$; $V = 699(2)$ Å$^3$, space group P2, $C_{15}H_{20}O_5$, $Z = 2$, $d = 1.33$ g/cm$^3$, $\lambda CuK_\alpha$ (graphite monochromator) $\mu = 7.9$ cm$^{-1}$, crystal size 0.045 × 0.09 × 1.3

TABLE 1. Coordinates (× $10^4$) and Equivalent Temperature Factors $U_{eq}$ (Å$^2$, × $10^3$) of the Nonhydrogen Atoms of Compound (**2**)

| Atom | $x/a$ | $y/b$ | $z/c$ | $U_{eq}$ |
|---|---|---|---|---|
| C1 | 1410(14) | 1854(13) | 1580(6) | 55(3) |
| C2 | 2500(13) | 396(14) | 1450(6) | 60(3) |
| C3 | 2290(12) | −392(12) | 2475(7) | 58(3) |
| C4 | 211(12) | 266(12) | 2955(6) | 51(3) |
| C5 | 477(14) | 1895(13) | 2700(6) | 52(3) |
| C6 | −1512(14) | 2856(12) | 2759(6) | 50(3) |
| C7 | −1046(14) | 4496(12) | 2781(7) | 59(3) |
| C8 | −635(16) | 5155(12) | 1714(7) | 68(3) |
| C9 | 1614(17) | 4733(13) | 1274(7) | 72(4) |
| C10 | 1912(14) | 3160(12) | 918(7) | 65(3) |
| C11 | −2994(16) | 5056(12) | 3343(7) | 70(3) |
| C12 | −3730(16) | 3822(14) | 4051(8) | 65(4) |
| C13 | −4083(18) | 6359(13) | 3345(9) | 92(4) |
| C14 | 3602(16) | 2978(14) | 93(7) | 80(4) |
| C15 | −114(13) | −98(13) | 4118(6) | 64(3) |
| O1 | −2651(9) | 2608(8) | 3763(4) | 56(2) |
| O2 | −4945(12) | 3849(9) | 4760(6) | 83(3) |
| O3 | −74(10) | 2315(8) | 704(4) | 64(2) |
| O4 | 4234(8) | −26(9) | 3122(4) | 66(2) |
| O5 | −1620(9) | −331 | 2313(4) | 61(2) |

TABLE 2. Intracyclic Torsional Angles (degrees) in the (**2**) Molecule

| Angle | | | | Value | Angle | | | | Value |
|---|---|---|---|---|---|---|---|---|---|
| C5 | C1 | C2 | C3 | 1.8(9) | C2 | C1 | C5 | C4 | 23.5(8) |
| C10 | C1 | C5 | C6 | −50(1) | C5 | C1 | C10 | C9 | −1(1) |
| C1 | C2 | C3 | C4 | −26.7(9) | C2 | C3 | C4 | C5 | 41.1(8) |
| C3 | C4 | C5 | C1 | −39.0(7) | C1 | C5 | C6 | C7 | 77(1) |
| C5 | C6 | C7 | C8 | −80.2(9) | O1 | C6 | C7 | C11 | 33.2(8) |
| C7 | C6 | O1 | C12 | −28.1(8) | C6 | C7 | C8 | C9 | 72(1) |
| C6 | C7 | C11 | C12 | −27.8(9) | C7 | C8 | C9 | C10 | −71(1) |
| C8 | C9 | C10 | C1 | 51(1) | C7 | C11 | C12 | O1 | 12(1) |
| C11 | C12 | O1 | C6 | 10.6(9) | | | | | |

mm$^3$. The quality of the crystals of (**2**) was low and the mosaicity high. The intensities of 1006 independent reflections with $2\theta < 114°$were measured by the ω-scanning method. The structure was interpreted by the direct method using the SHELX-86 program and was refined by the method of least squares in the full-matrix anisotropic – isotropic approximation by the SHELX-76 program to $R = 0.0486$ and $R_w = 0.0531$, $S = 1.11$ for 702 $F_0 > 4$ (F). Corrections for absorption were made by the DIFABS program (corrections 0.88-1.71). The positions of the hydrogen atoms were found from a difference synthesis and were not refined. The coordinates obtained for the nonhydrogen atoms are given in Table 1.

## REFERENCES

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