ARSANIN – A NEW SESQUITERPENE LACTONE FROM Artemsia santolina

B. Akyev, Sh. Z. Kasymov, and G. P. Sidyakin

UDC 547.913.5+547.473.2

We have previously reported the isolation from the epigeal part of Artemisia santolina Schrenk. of four sesquiterpene γ-lactones [1]. One of them, with the composition $C_{15}H_{22}O_4$, mol. wt, 266 (mass spectrometry), mp 193-194°C (from ethanol), $[\alpha]_D^{20}+26°$ (c 3.33; chloroform), proved to be new, and we have called it arsanin (I).

The IR spectrum of arsanin (Fig. 1a) has absorption bands in the regions of 3490 cm^{-1} (hydroxy group), 1770 cm^{-1} (carbonyl group of a γ-lactone ring), and 1705 cm^{-1} (ketone group in a six-membered ring). Arsanin is a saturated compound containing a hydroxy and an oxo group. The presence of a lactone ring in

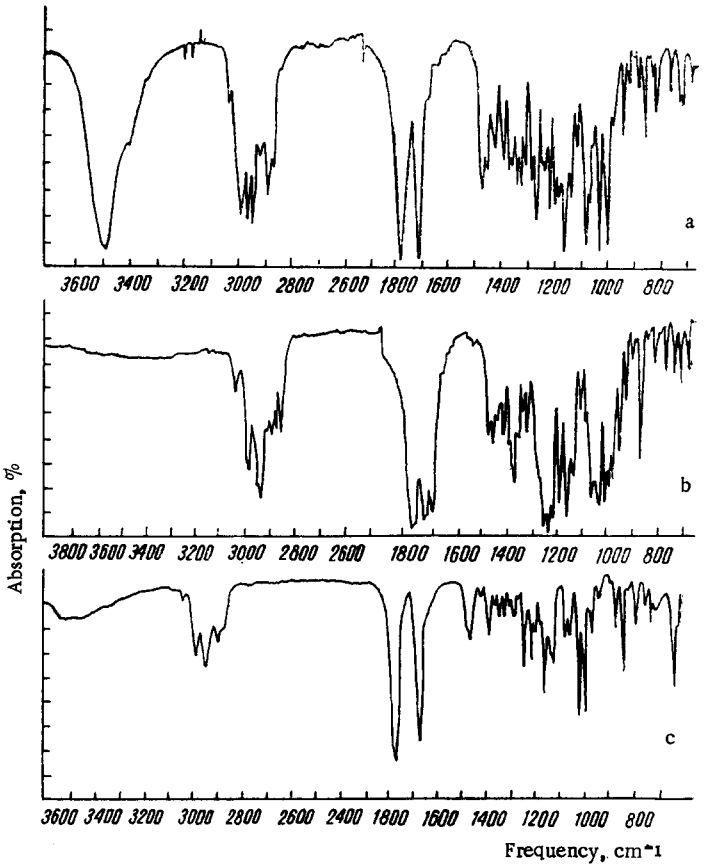


Fig. 1. IR spectrum of arsanin (a), acetylarsanin (b), and anhydroarsanin (c).

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 461-465, July-August, 1972. Original article submitted February 4, 1972.

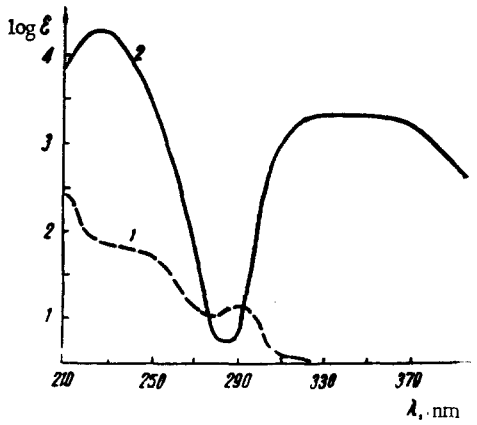


Fig. 2. UV spectra of arsanin (1) and of anhydroarsanin (2).

arsanin was confirmed by its solubility on heating in alkalis with its recovery in unchanged form from an acid medium.

The UV spectrum of the lactone (Fig. 2) lacks the system of bands typical for conjugation. A weak maximum at λ_{max} 290 nm (log ε 1.12) is due to an isolated carbonyl group [2].

In the NMR spectrum (here and below, the δ scale is used) of arsanin taken in [D]pyridine (Fig. 3a) there are signals in the methyl group region: a singlet at 1.12 ppm (3H) characteristic for an angular methyl group ($CH_3-\overset{|}{\underset{|}{C}}-$ при C_{10}), which shows the bicyclic nature of the arsanin skeleton, and doublets with centers at 1.08 ppm (3H, J = 6 Hz) and 1.28 ppm (3H, J = 7 Hz) relating to the methyl groups of secondary carbon atoms (> CH − CH_3). The signal of the lactone proton (H at C_5) in arsanin appears in the form of a triplet with its center at 3.76 ppm ($J_1 + J_2 = 20$ Hz); consequently, the lactone ring is located at C_5, C_6. A broadened signal at 4.68 ppm corresponds to the proton of a hydroxy group.

Arsanin is readily acetylated by acetic anhydride in the presence of pyridine, forming an acetyl derivative, $C_{17}H_{24}O_5$ (II), with mp 171°C (from ethanol). In the IR spectrum of this compound (Fig. 1b) there are absorption bands in the regions of 1779 cm^{-1} (γ-lactone carbonyl), 1740 and 1250 cm^{-1} (−OCOCH$_3$), and 1700 cm^{-1} (>C = O).

In the NMR spectrum of acetylarsanin (Fig. 3b) the signal of the angular methyl group appears in the form of a singlet at 1.14 ppm (3H, $CH_3-\overset{|}{\underset{|}{C}}-$ at C_{10}), and doublets with centers at 1.26 (3H, J = 5 Hz) and 1.20 ppm (3H, J = 4 Hz) relate to methyl groups on secondary carbon atoms (> CH − CH_3). A triplet with its center at 3.92 ppm (1H, $J_1 + J_2 = 20$ Hz) corresponds to the lactone proton at C_5. A singlet in the 2.01 ppm region (3H, −OCOCH_3) is due to the protons of an acetyl group. The proton attached to the carbon atom connected with the acetyl group gives a signal in the form of a quartet with its center at 4.74 ppm (J = 6 Hz) [3]. This shows that this proton is adjacent to the methylene group. Consequently, the hydroxy group is present at C_1.

In order to determine the positions of the oxo and hydroxy groups more accurately, we performed the elimination of the hydroxy group. On treatment with 50% sulfuric acid, arsanin readily loses a molecule of water, forming an anhydro derivative (III) with the composition $C_{15}H_{20}O_3$, mp 138-139°C (from ethanol). With vanillin in sulfuric acid, this substance gives a faint pink color.

The IR spectrum of (III) (Fig. 1c) has a maximum at 1765 cm^{-1} (γ-lactone carbonyl); it has no absorption band of a hydroxy group, and the band of the carbonyl group is shifted to 1665 cm^{-1}, which is characteristic for α,β-unsaturated ketones [4, 5].

The UV spectrum of anhydroarsanin has maxima at 227 and 330 nm (log ε 4.207 and 3.348, respectively). This shows the presence of an oxo group conjugated with a double bond [6, 7], which confirms the hypothesis that the hydroxy group in (I) is in the C_1 position and the ketonic carbonyl at C_3.

The NMR spectrum of (III) (Fig. 3, c) has the signals of an angular methyl group: a singlet at 1.11 ppm (3H, $CH_3-\overset{|}{\underset{|}{C}}-$); and a doublet with its center at 1.31 ppm (3H, J = 6 Hz) corresponding to a methyl group on a secondary carbon atom (> CH − CH_3). The signal of a third methyl group in the form of a doublet with its center at 1.17 ppm (3H, J = 6 Hz) at C_4 is superposed on the singlet of the angular methyl. The signal of the lactone proton in (III) appears in the form of a triplet with its center at 3.95 ppm (1H, J = 10 Hz). In the NMR spectrum of anhydroarsanin, unlike those of (I) and (II), two doublets (of one proton unit each) are found in the region of olefinic protons with their centers at 6.68 ppm (J = 10 Hz) and 5.88 ppm (J = 10 Hz).

Thus, arsanin belongs to the sesquiterpene γ-lactones of the eudesmane (selinane) type and is 1-hydroxy-3-oxoeudesm-5,12-olide.

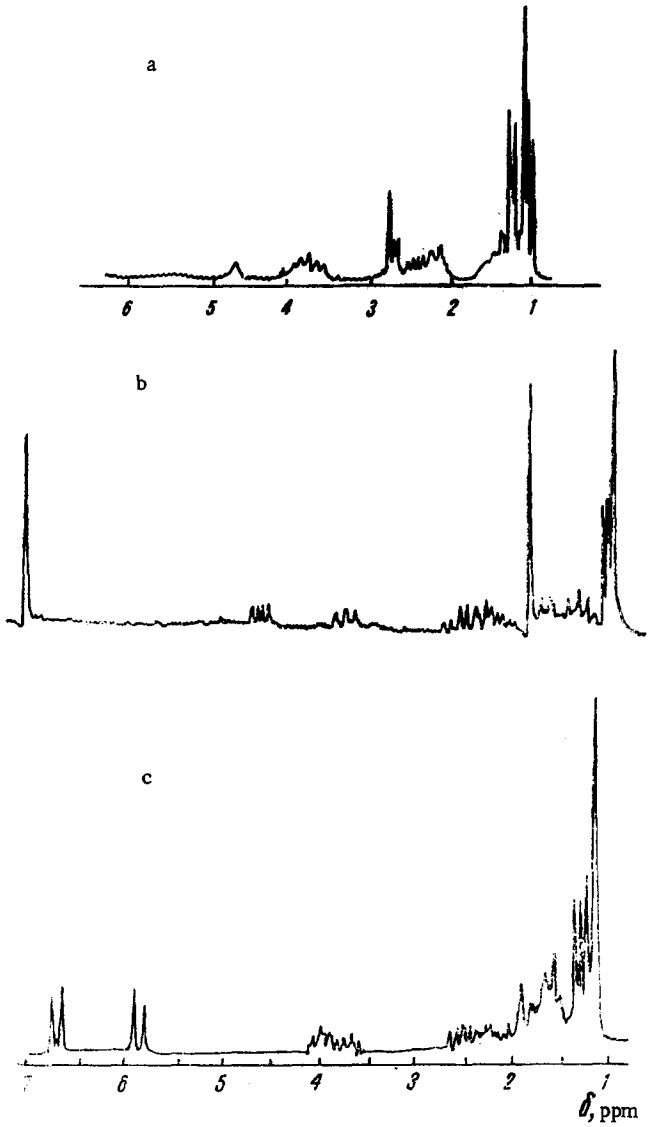
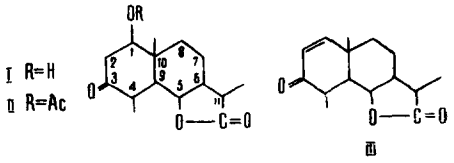


Fig. 3. NMR spectra of arsanin (a), acetylarsanin (b), and anhydroarsanin (c).



EXPERIMENTAL

The UV spectra were taken on a Hitachi spectrophotometer, the UR spectra on a UR-20 instrument (tablets with KBr), the mass spectra on an MKh-1303 mass spectrometer, and the NMR spectra on a JNH-4H-100 MHz instrument (the spectrum of arsanin was taken in [D]pyridine and those of the other substances in deuterochloroform), with HMDS as internal standard.

Thin-layer chromatography was performed with neutral alumina in the ethyl acetate system, the spots being revealed with iodine vapor and with a 1% solution of vanillin in 1% sulfuric acid.

The analyses of all the compounds corresponded to the calculated figures.

Arsanin (I). The epigeal part (unripe seeds, flowers, thin stems) of Artemisia santolina Schrenk. collected on August 23, 1970, in the south eastern Karakumy (Chardzhou oblast, Turkmen SSR) (23 kg) was

extracted with chloroform (7 × 70 liters). The combined extract was evaporated to dryness. This gave 2100 g of combined extractives (9.12% of the weight of the dry plant). This material was dissolved in 60% ethanol, and the ballast substances that deposited on standing were filtered off. The filtrate was extracted five times with chloroform. Distillation of the solvent yielded 720 g of resin (3.13% of the weight of the dry plant). The resin was dissolved in 50% ethanol, the precipitate was filtered off, and the filtrate was treated with ether to give 210 g (0.09% of the weight of the dry plant) of total lactones in the form of a light brown mass. The total lactones were passed through a column (92 × 5.3 cm^2) of alumina (neutral, activity grade III) in a ratio of 1:10. Elution was performed successively with petroleum ether, petroleum ether–benzene (8:2, 7:3, 1:1), benzene, benzene–ether (7:3, 1:1), ether, chloroform, and chloroform–methanol (95:5). The eluates were collected in 1-liter portions. The petroleum ether–benzene (1:1) fraction deposited 0.7 of crystals of arsanin with mp 193-194°C (from ethanol), R_f 0.37. With vanillin in sulfuric acid, the substance gave a faint brown coloration. Mol. wt. 266 (mass spectrometry).

Acetylarsanin (II). A solution of 0.2 g of arsanin in 4 ml of pyridine was treated with 4 ml of acetic anhydride. The mixture was left at room temperature for 15 h. The solvent was evaporated off under vacuum. The residue consisted of a substance with the composition $C_{17}H_{24}O_5$, mp 171°C (from ethanol), R_f 0.69. Mol. wt. 308 (mass spectrometry).

Anhydroarsanin (III). A solution of 0.1 g of arsanin in 20 ml of 50% sulfuric acid was heated in the water bath at 60-70°C for 5 min. The mixture was diluted with water, neutralized with sodium carbonate, and extracted five times with chloroform. The solvent was distilled off, and the residue was purified on a column of silica gel (1:10). Elution was performed with petroleum ether, benzene, and chloroform. The chloroform eluates gave crystals with the composition $C_{15}H_{20}O_3$, mp 138-139°C (from ethanol), R_f 0.63. Mol. wt. 248 (mass spectrometry).

SUMMARY

From the epigeal part of Artemisia santolina Schrenk. has been isolated a new sesquiterpene lactone, arsanin, $C_{15}H_{22}O_4$, which has the structure of 1-hydroxy-3-oxoeudesm-5,12-olide.

LITERATURE CITED

1. B. Akyev, Sh. Z. Kasymov, and G. P. Sidyakin, Khim. Prirodn. Soedin., 531 (1961).
2. J. Brand and G. Eglinton, Applications of Spectroscopy to Organic Chemistry, Oldbourne Press, London (1965).
3. K. S. Rybalko, A. I. Ban'kovskii, and V. I. Sheichenko, Lekarstv. Rast., 15, 234 (1969).
4. W. West, Chemical Applications of Spectroscopy, Interscience, New York (1956).
5. L. Bellamy, Infra-Red Spectra of Complex Molecules, Methuen (1958).
6. T. A. Geissman, T. S. Griffin, and M. A. Irwin, Phytochemistry, 8 (7), 1297 (1969).
7. J. Bermejo Barrera, J. L. Breton, M. Fajardo, and A. G. Gonzales, Tetrahedron Lett., No. 36, 3475 (1967).