ARTEMOLIN — A NEW GUAIANOLIDE FROM *Artemisia absinthium*

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The epigeal part of *Artemisia absinthium* L. has yielded a new sesquiterpene lactone artemolin, $C_{15}H_{20}O_5$, with mp 205°C, $[\alpha]_D^{20}$ +18° (c 1.0, chloroform). The structure of artemolin has been established on the basis of chemical transformations and spectral characteristics.

In a study of the sesquiterpene lactones of *Artemisia absinthium* L. (common wormwood), family Compositae, we have isolated a new lactone artemolin (I), $C_{15}H_{20}O_5$, mp 205°C, $[\alpha]_D^{20}$ +18° (c 1.0; chloroform); M^+ 280.

The UV spectrum of (I) has a maximum at 223 nm (log ε 4.07) which is due to the presence of an α,β-unsaturated carbonyl group. The IR spectrum of artemolin (Fig. 1) shows absorption bands at (cm^{-1}) 3430 and 3470 (OH groups), 1770 (C=O of a γ-lactone ring), 1700 (C=C—C=O), and 1635 (C=C).

The ^1H NMR spectrum of artemolin shows the signals of three methyl groups: a doublet at 1.01 ppm (^3J = 6.7 Hz) $(-\overset{|}{C}H-CH_3)$, and singlets at 1.58 and 1.68 ppm $[2(HO-\overset{|}{\underset{|}{C}}-CH_3)]$. The signal of a methine proton geminal to a lactone oxygen atom (lactone proton) is represented in the form of a doublet at 5.82 ppm with ^3J = 8.8 Hz. At 6.13 and 6.28 ppm there are singlet signals of two tertiary hydroxy groups. One-proton doublets with ^2J = 18.3 Hz at 2.50 and 2.85 ppm are characteristic for the protons of an isolated methylene group [1] located in the α-position relative to a carbonyl group.

The ^{13}C NMR spectrum of artemolin with incomplete decoupling from protons (off-resonance) has — in addition to the signals of two carbonyl carbon atoms — singlet signals at 143.2 and 171.9 ppm which are characteristic for sp^2-hybridized carbon atoms. The presence of these signals shows that the molecule of (I) has one tetrasubstituted double bond.

The exchange of the mobile hydrogen atoms of the artemolin molecule with deuterium led to an increase in its molecular weight by two mass units.

Thus, artemolin has two tertiary hydroxy groups and an α,β-unsaturated carbonyl group.

The hydrogenation of (I) in the presence of platinum oxide in ethanol led to tetrahydroartemolin (II), $C_{15}H_{24}O_5$, mp 233°C. In contrast to the initial lactone, the IR spectrum of (II) lacked the absorption band due to an α,β-unsaturated carbonyl group. When the ^1H NMR spectra of (I) and (II) were compared, it was seen that in the spectrum of (II) the position and nature of the splitting of the signal of the lactone proton had changed. It appeared in a stronger field at 4.91 ppm in the form of a triplet with ^3J about 9 Hz. These facts show that one of the carbon atoms of the tetrasubstituted double bond is located in the α-position relative to the C_6—H lactone proton. Consequently, in this reaction the carbonyl group is reduced simultaneously with the hydrogenation of the double bond.

The action of acetyl chloride on artemolin gave compound (III), $C_{15}H_{18}O_4$, mp 229-230°C.

The IR spectrum of (III) showed absorption bands at (cm^{-1}) 3320 (OH group), 1775 (C=O of a γ-lactone ring), 1675 (dienone grouping), and 1630 and 1625 (C=C bond). The presence of a dienone grouping in the molecule of (III) was confirmed by its UV spectrum, which contained a maximum at 247 nm (log ε 4.16), as in leucomisin [2]. The ^1H NMR spectrum of (III)

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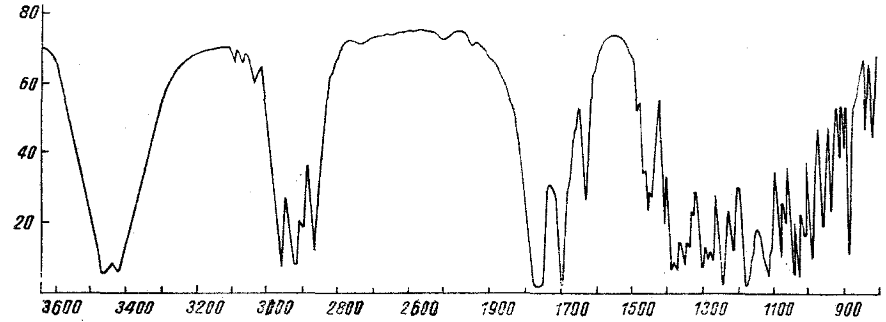
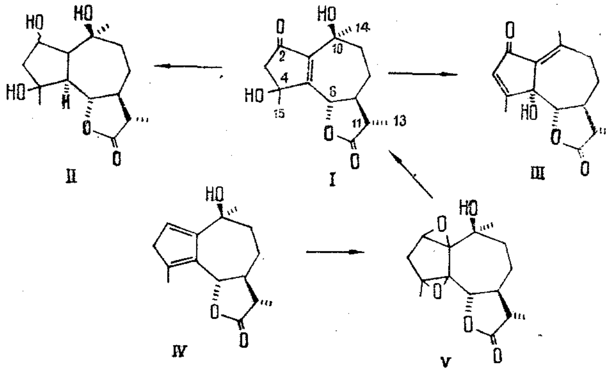


Fig. 1. IR spectrum of artemolin.

($CDCl_3$) showed the signals of three methyl groups: doublet at 1.20 ppm with $^3J = 6.5$ Hz ($-\overset{|}{C}H-CH_3$) and singlets at 2.21 and 2.34 ppm $[2(-\overset{|}{C}=\overset{|}{C}-CH_3)]$. The signal of the lactone proton appeared in the form of a doublet at 3.83 ppm with $^3J = 10$ Hz. The signal of an olefinic proton was observed at 6.03 ppm.

All the spectral characteristics and physicochemical constants of compound (III) agree with those of the lactone parishin C which has been described in the literature [3]. The configuration of the hydroxy group at C_{10} was determined by a comparative analysis of the chemical shifts of the protons at C_6 and C_7 using a shift reagent. On the basis of the facts given, artemolin has the structure (I):



In the plant, artemolin is apparently formed from artabsin (IV) [4] via the epoxy compound (V).

EXPERIMENTAL

The UV spectra were taken on a Hitachi spectrophotometer in ethanol, the IR spectra on a UR-20 instrument (tablets with KBr), the mass spectra on a MKh 1303, and the ^1H NMR spectra of (I) and (II) in deuteropyridine solution and of (III) in $CDCl_3$ on a JNM-4H-100 spectrometer with 0 — HMDS. The ^{13}C NMR spectra of (I) were recorded in deuteropyridine on a Varian CFT-20 spectrometer with 0 — TMS. The individuality of the compounds was determined with the aid of TLC on alumina in ethyl acetate.

Isolation of Artemolin (I). The leaves and inflorescences of *Artemisia absinthium* (20 kg) collected in June, 1976, in Tashkent province were extracted with ether. The extract was evaporated and the residue was dissolved in 60% aqueous ethanol. The aqueous ethanolic solution was treated with chloroform and the concentrated chloroform extract (170 g) was chromatographed on alumina (activity grade IV). Elution was carried out with petroleum ether–benzene (1:1) and with benzene. The benzene fractions, on being treated with acetone, deposited crystals of artemolin (0.4 g), $C_{15}H_{20}O_5$, mp 205°C (benzene–acetone), $[\alpha]_D^{20}$ +18° (c 1.0; chloroform). Artemolin was deuterated in CD_3OD. The molecular weight of the deuteroartemolin was 282, R_f 0.53. When treated on TLC plates with vanillin in concentrated sulfuric acid, artemolin was colored pink.

UV spectrum: $\lambda_{max}^{C_2H_5OH}$ 223 nm (log ε 4.07) $(-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}=O)$. IR spectrum, ν_{max}^{KBr}, cm^{-1}: 3430, 3470 (OH group), 1770 (C=O of a γ-lactone ring), 1705 $(\overset{|}{C}=\overset{|}{C}-\overset{|}{C}=O)$, 1635 (C=C bond). ^1H NMR spectrum, ppm: doublet at 1.01 with ^3J = 6.7 Hz $(-CH-CH_3)$, singlets at 1.58 and 1.68 $[2(HO-C-CH_3)]$, doublet at 5.82 with ^3J = 8.8 Hz (—O—CH), doublets at 2.50 and 2.85 ppm with ^2J = 18.3 Hz $(O=C-CH_2)$.

Tetrahydroartemolin (II). Artemolin (0.15 g) was dissolved in 25 ml of ethanol, 0.02 g of platinum oxide was added, and hydrogenation was carried out for 1.5 h. The catalyst was filtered off and the solvent was evaporated off. The residue was chromatographed on alumina with elution by benzene, benzene—ether (19:1), ether, and ether—ethyl acetate (4:1). The last fractions deposited crystals of tetrahydroartemolin (0.05 g), $C_{15}H_{24}O_5$, mp 233°C (ethyl acetate); M 284 (mass spectrometry); R_f 0.41. Vanillin in concentrated sulfuric acid colored (II) deep blue.

IR spectrum, ν_{max}^{KBr}, cm^{-1}: 3200-3300 and 3560 (OH groups), 1765 (C=O of a γ-lactone ring). ^1H NMR spectrum, ppm: doublet at 1.06 with ^3J = 6.6 Hz $(-CH-CH_3)$, singlets at 1.40 and 1.85 $[2(HO-C-CH_3)]$, triplet at 4.91 with ^3J = 9 Hz $(-O-\overset{|}{C}H-)$.

Preparation of Parishin C. A solution of 0.1 g of artemolin in 18 ml of acetyl chloride was heated at 40°C for 2 h. Then the solvent was evaporated off and the product was chromatographed on alumina. The eluates obtained with benzene—ether (9:1) yielded parishin C (0.03 g), $C_{15}H_{18}O_4$, mp 229-230°C (benzene). UV spectrum, $\lambda_{max}^{C_2H_5OH}$: 247 nm (log ε 4.16) $(C=C-C(=O)-C=C)$. IR spectrum, ν_{max}^{KBr}, cm^{-1}: 3320 (OH group), 1775 (C=O of a γ-lactone ring), 1675 $(C=C-C(=O)-C=C)$, 1630 and 1628 (C=C bond). ^1H NMR spectrum $(CDCl_3)$, ppm: doublet at 1.20 with ^3J = 6.5 Hz, singlets at 2.21 and 2.34 $[2(C=C-CH_3)]$, doublet at 3.83 with ^3J = 10 Hz (—O—CH), broadened singlet at 6.03 ppm (HC=C<).

SUMMARY

The new guaianolide artemolin has been isolated from *Artemisia absinthium* L.

Its structure has been established on the basis of chemical transformations and spectral characteristics.

LITERATURE CITED

1. F. Bohlmann, P. K. Mahanta, and L. N. Dutta, Phytochemistry, 18, 289 (1979).
2. K. S. Rybalko, Zh. Obshch. Khim., 33, 2734 (1963).
3. H. Yoshioka, T. Mabry, and B. Timmerman, Sesquiterpene Lactones, University of Tokyo Press (1973), p. 349.
4. K. Vokač, Z. Samek, V. Herout, and F. Sorm, Collect. Czech. Chem. Commun., 37, 1346 (1972).