STRUCTURE OF ARTABIN

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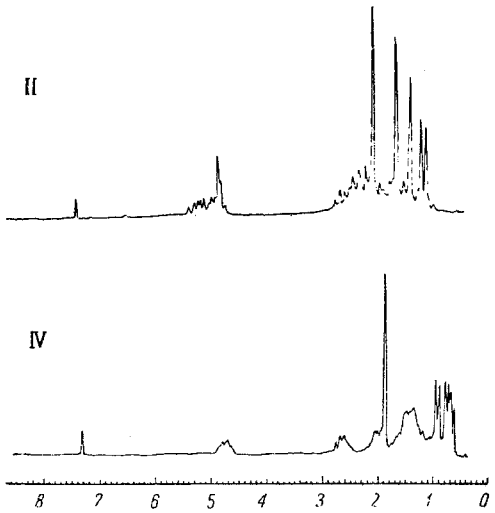
The isolation of a new sesquiterpene lactone artabin (I) from Artemisia absinthium L. has been reported previously. The composition, spectral characteristics, and other properties showed that artabin was a lactone of the germacrane type [1].

Continuing our investigation of the structure of artabin, we have studied the spectra and properties of its derivatives: acetylartabin (II) and tetrahydroartabin (III).

The NMR spectrum (δ scale) of acetylartabin has the signals of a secondary methyl (doublet at 1.19 ppm, J = 9 Hz) and singlets at 1.45 and 1.61 ppm corresponding to methyl groups on double bonds. The signal of the methyl of an acetyl group appears at 2.03 ppm in the form of a singlet and the lactone proton at 4.76 ppm.

The catalytic hydrogenation of acetylartabin (II) gave tetrahydroacetylartabin (IV) in the IR spectrum of which there are absorption bands at 1760 cm^{-1} (γ-lactone) and 1722 and 1250 cm^{-1} (acetyl group). The NMR spectrum of compound IV has the signals of secondary methyls (doublets at 0.63 ppm, J = 7 Hz, 0.74 ppm, J = 7 Hz, and 0.88 ppm, J = 8 Hz). The singlet at 1.75 ppm corresponds to the methyl of an acetyl group, and a two-proton signal in the form of an unresolved multiplet at 4.50 ppm to the lactone proton at C_6 and to a proton at C_3 (Fig. 1).

The hydrogenation of artabin in the presence of PtO_2 and $HClO_4$ in acetic acid did not give a cyclized product. This can be explained as follows: while in other lactones of the germacrane type (dihydrocostunolide, balchanolide, and others) on cyclization under the conditions mentioned [2] the double bond at $C_4 - C_5$ migrates in the $C_3 - C_4$ position, in the case of artabin there is a hydroxy group at C_3, which opposes the migration of the double bond.



We effected the cyclization of artabin by heating it with 50% sulfuric acid. The cyclization product was identical with tetrahydro-β-santonin (V). The latter has been obtained from β-santonin (VI) [3]. The

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Scheme of the transformations of artabin

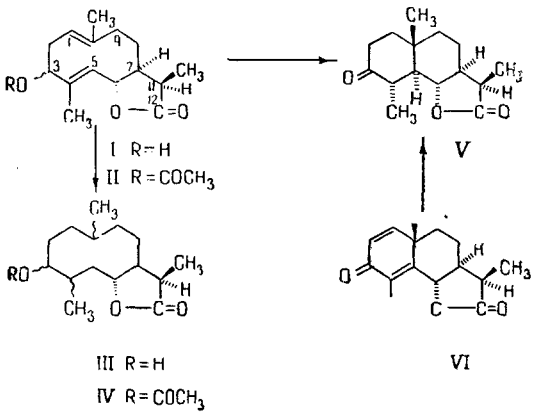

Fig. 1. NMR spectra of acetylartabin (II) and tetrahydroacetylartabin (IV).

IR spectra of the two compounds were identical, and a mixture gave no depression of the melting point. The 2,4-dinitrophenylhydrazones of both compounds were also obtained and shown to be identical.

Consequently, the lactone ring of artabin has the same configuration as in β-santonin, and its hydroxy group is located at C_3.

EXPERIMENTAL

The NMR spectra were taken on a JNM-4H-100/100 MHz instrument (in $CDCl_3$).

Isolation of Artabin (I). A 27-kg sample of the epigeal part of the plant (collected in August, 1969) was extracted three times with hot water (80°C, 30 min). The aqueous extract was shaken with chloroform, and the solvent was distilled off. The residue (110 g) was triturated with ether. The resins remaining after the ether had been distilled off were dissolved in ethanol, and sufficient water was added to give a 60% aqueous ethanolic solution. This solution was washed with petroleum ether, the ethanol was distilled off, and the lactones were extracted with chloroform. The residue from the chloroform was chromatographed on a column (600 g) of acid alumina (activity grade IV). The benzene solutions, after the solvent had been distilled off and a small amount of ether had been added, yielded crystals of artabin (5.4 g), $C_{15}H_{22}O_3$, mp 162-164°C (from benzene–petroleum ether), $[\alpha]_D^{20}$ + 220 (c 1.5; ethanol), mol. wt. 250 (mass spectrometry).

Acetylartabin (II). A mixture of 100 mg of artabin, 2 ml of pyridine, and 2 ml of acetic anhydride was stirred for 12 h, and then water was added. Ether isolated 70 mg of acetylartabin, $C_{17}H_{24}O_4$, mp 172-173°C (from ethanol), mol. wt. 292 (mass spectrometry).

Tetrahydroartabin (III). In the presence of 42 mg of platinum oxide (Adams), 150 mg of artabin in 20 ml of ethanol was hydrogenated until the absorption of hydrogen ceased. The catalyst was filtered off and the solvent was distilled off. The yield of tetrahydroartabin was 100 mg, composition $C_{15}H_{26}O_3$, mp 153-154°C (from benzene), mol. wt. 254 (mass spectrometry).

Tetrahydroacetylartabin (IV). Under the conditions for the preparation of III, 400 mg of acetylartabin in 50 ml of ethanol was hydrogenated with 0.1 g of platinum oxide (Adams). The yield of tetrahydroacetylartabin was 250 mg, composition $C_{17}H_{28}O_4$, mp 107-108°C (from petroleum ether), mol. wt. 296 (mass spectrometry).

Cyclization of Artabin. A mixture of 190 mg of artabin and 10 ml of 50% sulfuric acid was heated in the water bath for 5 min. The solution was cooled, diluted with a fivefold amount of water, and shaken with chloroform. The chloroform extracts were washed with 3% $NaHCO_3$ and then with water to neutrality. Distillation of the chloroform left 80 mg of tetrahydro-β-santonin (V), $C_{15}H_{22}O_3$, mp 123-124°C, mol. wt. 250 (mass spectrometry).

The 2,4-dinitrophenylhydrazone of cycloartabin (V) was obtained by mixing an ethanolic solution of the substance with a saturated solution of 2,4-dinitrophenylhydrazine. Crystals deposited in the form of yellow needles with mp 224-225°C (from ethanol).

SUMMARY

From Artemisia absinthium L. a new sesquiterpene lactone of the germacrane type – artabin – has been isolated. Structure I is proposed for it.

LITERATURE CITED

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3. Masaiti Yanagita Haruo Ogura, J. Organ. Chem., 23, No. 9, 1268, 1958.