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THE STRUCTURE OF ERIVANIN

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From the leaves and flower heads of Artemisia fragrans Willd., var. erivanica Bess., we have isolated a new sesquiterpene lactone, erivanin, with the composition $C_{15}H_{22}O_4$, mp 203-205° C (from benzene), $[\alpha]_D^{20}$ +112° (c 3.9; ethanol) [1].

The IR spectrum of the substance has absorption bands at 1762 cm^{-1} (carbonyl of a γ-lactone ring), 3444 cm^{-1} (OH group), and 1675 cm^{-1} (double bond).

The presence of a lactone ring in erivanin is confirmed by its solubility in alkali on heating. The acetylation of erivanin gave a diacetyl derivative $C_{19}H_{26}O_6$ with mp 192-193° C (from ethanol). Its IR spectrum had absorption bands at 1766 cm^{-1} (γ-lactone carbonyl), 1745 and 1262 cm^{-1} (acetyl group), and 1660 cm^{-1} (C=C bond).

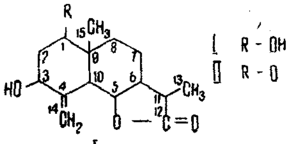
The lactone contains one double bond, as was found by its hydrogenation in the presence of a Pt catalyst. The dehydrogenation of erivanin over Se at 280-320° C for 30 hr gave 6-ethyl-1-methylnaphthalene, identified through its picrate, mp 94-96° C (from ethanol), and by the absence of a depression of the melting point in admixture with an analogous sample obtained by the dehydrogenation of tauremisin.

Thus, the hydrocarbon skeleton of erivanin is the same as that of santonin, tauremisin, and alantolactone, i.e., the substance is a sesquiterpene lactone of the eudesmane type; it contains one double bond and two OH groups.

The NMR spectrum of the lactone has the signals of a quaternary methyl (singlet at 0.79 ppm) and a tertiary methyl (doublet at 1.2 ppm, J = 7 Hz), and broadened singlets at 4.95 and 5.13 ppm corresponding to the protons of an exocyclic methylene. The positions of the signals show that the double bond is not located at C_{11}-C_{13} [2, 3] and it can therefore be only in the C_4—C_{14} position. The signal of the lactone proton (H at C_5) in erivanin appears in the form at a triplet at 4.06 ppm ($J_{5,6} + J_{5,10}$ = 20 Hz), from which it follows that the lactone ring is located at C_5—C_6. Two signals in the 3.37 and 4.36 ppm regions show the presence in the lactone of two other protons attached to a carbon atom with an OH group. Thus in erivanin the two hydroxyls are secondary. The comparatively high value of the chemical shift of one of these protons can be explained by the fact that one OH group is located in the α-position to the double bond.

In the NMR spectrum of the product of the oxidation of erivanin II the signal of the angular methyl group has been shifted comparatively strongly (by more than 0.25 ppm) into the weak field. This permits the conclusion that the second OH group is present in the α-position to the angular methyl. The value of the latter (1.12 ppm) is extremely close to that for tauremisin and taurin, which contain an oxo group in position 1.

On the basis of the results obtained, the following structure (I) may be proposed as the most probable for erivanin.



I

Experimental

Isolation of erivanin. The plant was collected in August 1965 in the Nakhichevan ASSR in the Shakhbuz region at the village of Badamly. R. I. Abbasov determined the plant as Artemisia Popovii Rzazade [4]. However, in view of the fact that this species of wormwood was not recognized in "Flora of the USSR" [5], it was ascribed to Artemisia fragrans Willd., var. erivanica Bess.

The leaves and flower heads were steeped in hot water (80-85° C) for 30 min three times. The aqueous extract was treated with chloroform and the latter was evaporated. The residue was treated with ether. The crystals that deposited (yield 0.01%) were recrystallized from benzene, mp 203-205° C, $[\alpha]_D^{20}$ +112° (3.9; ethanol).

Found, %: C 67.57, 67.38; H 8.54, 8.36; mol. wt. 251, 280 (cryoscopically). Calculated for $C_{15}H_{22}O_4$, %: C 67.66; H 8.27; mol. wt. 266.

The resin after the isolation of the erivanin was chromatographed on neutral Al_2O_3 (activity grade IV) and eluted with petroleum ether, a mixture of petroleum ether and benzene, and benzene. An additional amount of erivanin was obtained from the benzene fraction. The total yield was 0.05%.

Acetylerivanin. A mixture of 0.4 g of erivanin, 4 ml of acetic anhydride, and 8 ml of pyridine was heated at 60° C for 1 hr and was then diluted with water. The crystals that deposited were washed with water and recrystallized from ethanol to give 0.3 g of colorless crystals with mp 192–193.5° C.

Found, %: C 64.91; 65.31; H 7.59, 7.40. Calculated for $C_{19}H_{26}O_6$, %: C 65.14; H 7.42.

Dihydroerivanin. A solution of 0.17 g of erivanin in 50 ml of ethanol was treated with 0.05 g of PtO_2 (Adams) and was hydrogenated for 3 hr. The reaction product was extracted in the usual way, giving colorless crystals (0.1 g) with mp 219–221.5° C (from benzene and ethanol).

Found, %: C 67.33, 67.44; H 9.06, 9.04. Calculated for $C_{15}H_{24}O_4$, %: C 67.14; H 8.94

Oxidation of erivanin. A solution of 0.19 g of erivanin in 1.5 ml of pyridine was treated with a solution of 0.19 g of CrO_3 in 3.5 ml of pyridine and left at 0° C. After a day, the reaction mixture was diluted with water and the reaction product was extracted with a mixture of benzene and ether (1:1); the extract was washed with water, with 5% HCl solution, and with water again, the solvent was evaporated off, and the residue was washed with ether and recrystallized from benzene. This gave 0.1 g of colorless crystals with mp 178–183° C. IR spectrum: ν_{max}, cm^{-1}: 3520, 3480 (OH), 1780 (γ-lactone), 1722 (C = 0).

Dehydrogenation of erivanin. A mixture of 2 g of erivanin and 1 g of selenium was heated at 300–320° C for 30 hr. The reaction product was extracted with petroleum ether and the residue after the elimination of the solvent was fractionated at 2 mm Hg. The first highly mobile fraction was purified on neutral Al_2O_3 (activity grade I, petroleum ether). After the evaporation of the eluate the liquid substance was distilled over Na at 2 mm Hg. This gave 0.09 g of colorless liquid with n_D^{18} 1.5470 which was dissolved in 1 ml of absolute ethanol and mixed with a solution of 0.05 g of picric acid in absolute ethanol. Orange needles deposited. After recrystallization from ethanol, mp 94–96° C.

Found, %: C 56.91, 56.74; H 4.23, 4.44; N 10.38, 10.31. Calculated for $C_{13}H_{14} \cdot C_6H_3N_3O_7$, %: C 57.14; H 4.26; N 10.52.

Conclusions

From Artemisia frangrans Willd. var. erivanica Bess. a new sesquiterpene lactone, erivanin, has been isolated. Structure I has been proposed as the most probable for it.

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