ARTEMIDIOL — A NEW ISOCOUMARIN FROM Artemisia dracunculus

A. Mallabaev and G. P. Sidyakin

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Continuing a study of the lactones of chloroform extracts of the roots of Artemisia dracunculus L. [1-3] collected in the Oshk oblast, by chromatography we have detected artemidin and have isolated a crystalline substance with the composition $C_{13}H_{14}O_4$, mp 131.5-133°C, M^+ 234, which we have called artemidiol (I).

The substance dissolves readily in acetone and ethanol and, on heating, in alkalis, chloroform, benzene, ethyl acetate, and water and is insoluble in petroleum ether; it has R_f 0.4 [TLC, silica gel, chloroform–ether (7 : 3) system], is not stained by diazotized sulfanilamide, and can be revealed with a solution of potassium permanganate and with iodine vapor.

The UV spectrum of artemidiol shows maxima at 231, 242, 256 (shoulder), 265, 275, and 328 nm (log ε 4.30, 4.05, 3.70, 3.80, 3.70, and 3.30, respectively), which are characteristic for lactones of the isocoumarin series [3-5].

In the IR spectrum (Fig. 1a) there are absorption bands at 3420 (hydroxy group), 1712 (lactone carbonyl), 1660 (vinyl double bond) and 1608 and 1570 cm^{-1} (aromatic nucleus). The last four absorption bands, with a characteristic ratio of their intensities, show that the substance belongs to the isocoumarin group [6]. In addition to the frequencies mentioned, there is a band at 770 cm^{-1} (1,2-disubstituted benzene ring).

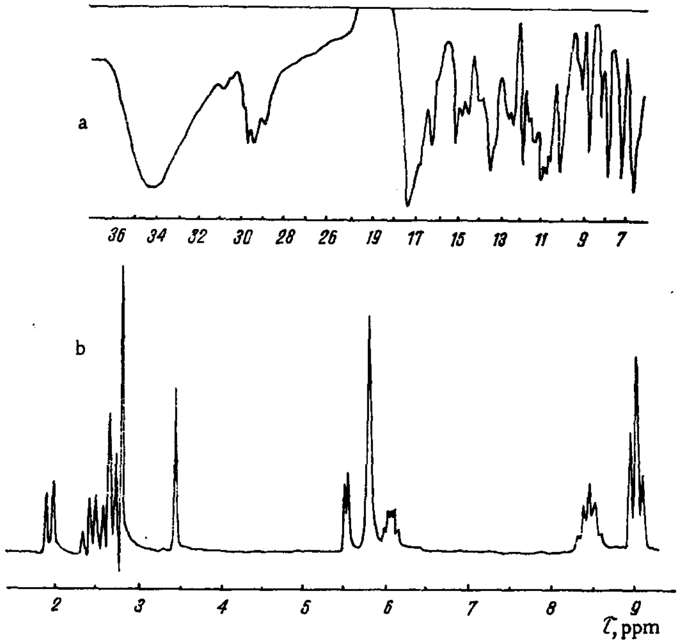

Fig. 1. IR spectrum (a) and NMR spectrum (b) of artemidiol.

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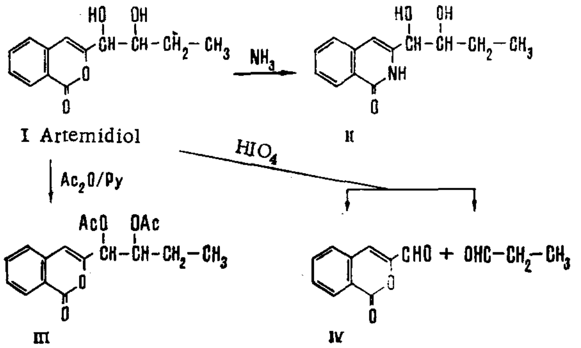
The indications of the UV and IR spectra of the isocoumarin nature of artemidiol were confirmed by the production of an isocarbostyril (II), $C_{13}H_{15}O_3N$, with mp 135-136°C. In the IR spectrum of this compound the frequency of the stretching vibration of the carbonyl group is lowered, and it appears at 1650 cm^{-1}, which is due to the influence of the adjacent NH group.

In the NMR spectrum of artemidiol (I) (Fig. 1b) a doublet at 1.88 ppm (1 H, $J=7.5$ Hz) and a multiplet with its center at 2.56 ppm (3 H) relate to the protons of a benzene ring the presence of which is confirmed by the band at 770 cm^{-1} in the IR spectrum [2]. In addition, a doublet at 5.45 ppm (1 H, $J_1=5$ Hz) and a complex sextet with its center at 6.00 ppm (1 H, $J_1=5$ Hz and $J_2=J_3=7.5$ Hz) relate to the signals of the protons of a $-CH-CH-$ group, and a quintet at 8.50 ppm (2 H, $J=7.5$ Hz) and a triplet at 9.08 ppm (3 H, $J=7.5$ Hz) correspond to the protons of an ethyl group. The multiplicity of the signal of the methine group (6.00 ppm) shows that it is located next to a methylene group. A singlet at 5.70 ppm with an intensity of two proton units corresponds to the signals of the protons of two hydroxy groups.

The acetylation of artemidiol with acetic anhydride in pyridine formed a diacetyl derivative (III), $C_{17}H_{18}O_6$, mp 73-74°C, M^+ 318.

The IR spectrum of diacetylartemidiol lacked the absorption band of a hydroxy group, but a strong band had appeared at 1737 cm^{-1} (lactone and acetyl carbonyls).



In the NMR spectrum of (III), unlike that of (I) there was no signal at 5.70 ppm, but two three-proton singlets had appeared at 7.90 and 8.00 ppm, belonging to the protons of acetyl groups. Furthermore, paramagnetic shifts of the signals of the protons of the methine groups of 1.08 and 1.24 ppm, respectively, were observed. The displacement of these signals shows that the hydroxy groups are secondary. Consequently, the side chain of artemidiol has the structure $-CHOH-CHOH-CH_2-CH_3$. The position of branching of the side chain and the locations of the hydroxy groups were established by the oxidation of artemidiol with periodic acid. This gave aldehyde (IV) which, from its IR spectrum, R_f value, and a mixed melting point was identical with artemidinal.

Thus, artemidiol has the structure of 3-(1',2'-dihydroxybutyl)isocoumarin.

EXPERIMENTAL

The IR spectra were taken on a UR-10 spectrophotometer (tablets with KBr), the mass spectra on a MKh-1303 mass spectrometer, and the NMR spectra on a JNM-4H-100 MHz spectrometer (in $CDCl_3$; the chemical shifts are given in the τ scale from the signal of HMDS taken as 10), and the UV spectra on a Hitachi spectrophotometer.

Isolation of Artemidiol. The roots (16 kg) were extracted with chloroform, and 150 g of the extract was chromatographed on neutral alumina (activity grade III, ratio 1 : 10). The column was washed successively with petroleum ether, diethyl ether, and methanol. The diethyl ether fraction was rechromatographed on silica gel (KSK, in a ratio of 1 : 20). Elution was performed with benzene, benzene–chloroform mixtures (9 : 1, 3 : 1, 1 : 1, and 1 : 3), chloroform, and chloroform–ether (4 : 1), 750-ml fractions of the eluate being collected. From the benzene eluates (3-13) artemidin was found chromatographically [TLC on silica gel in the petroleum ether–diethyl ether (9 : 1) system], and from the chloroform–ether (4 : 1) eluates (83-86) we isolated 0.4 g of artemidiol with mp 131.5-133°C (from benzene and ethyl acetate).

Amination of Artemidiol. A mixture of 50 mg of artemidiol and 2 ml of concentrated ammonia was heated in a sealed tube in the water bath for 5 h. Then the contents of the tube were treated with ether, and the distillation of the solvent from the extract yielded 33 mg of crystals with mp 135-136°C (from benzene), R_f 0.5 (silica gel, chloroform–ether (20 : 1) system).

Acetylation of Artemidiol. A mixture of 100 mg of artemidiol and 2 ml of a solution of acetic anhydride in pyridine (1 : 1) was left for 12 h, after which it was diluted with water and extracted with ether. The solvent was driven off under vacuum and the residue was separated by preparative chromatography in a fixed layer of silica gel in the hexane–ethyl acetate (3 : 1) system. The band with R_f 0.4-0.6 was separated off, and from it 62 mg of diacetate with mp 73-74°C (from petroleum ether) was eluted with chloroform and methanol.

Oxidation of Artemidiol by Periodic Acid. To 10 g of artemidiol was added 2 ml of aqueous ethanol (1 : 3) containing 15 mg of periodic acid, and the mixture was left for 12 h. Then it was treated with chloroform, the solvent was distilled off, and the residue was separated by preparative chromatography in a fixed layer of silica gel in the chloroform–ether (9 : 1) system. The section with R_f 0.5 was separated off, and from it ether extracted artemidinal (6 mg) with mp 175-176°C (from benzene).

SUMMARY

The roots of *Artemisia dracunculus* L. have yielded a new isocoumarin – artemidiol – with the composition $C_{13}H_{14}O_4$, mp 131.5-133°C, which has the structure of 3-(1'-2'-dihydroxybutyl)isocoumarin.

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