THE STRUCTURE OF ARNIFOLIN

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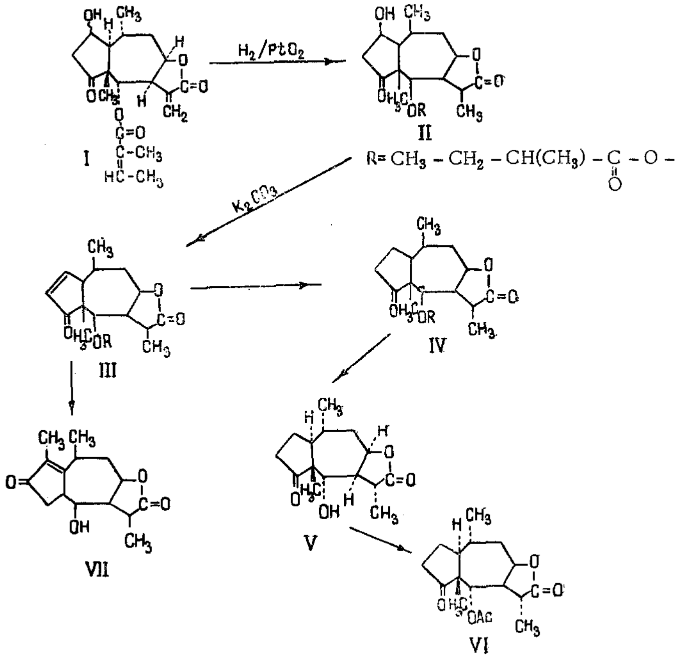
As reported previously [1] the probable structure (I) has been suggested for arnifolin – a sesquiterpene lactone isolated from Arnica montana L. and A. foliosa Nutt. At the present time, we have obtained new experimental results confirming this structure and characterizing its stereochemistry.

The hydrogenation of anhydrotetrahydroarnifolin (III) in the presence of a Ni catalyst gave the dihydro derivative (IV), from which hydrolysis formed substance (V) with the composition $C_{15}H_{22}O_4$, mp 170-171.5°C, $[\alpha]_D^{20}+119°$ (c 2.1; chloroform). IR spectrum, ν_{max}, cm^{-1}: 3430 (OH), 1770 (γ-lactone), 1740 (cyclopentanone). NMR spectrum: singlet at 1.06 ppm (CH_3 at C_{10}), two doublets at 1.14 and 1.40 ppm (CH_3 at C_8 and C_{11}), doublet at 4.32 ppm (H_4), and multiplet at 4.87 ppm (H_6).

With acetic anhydride, (V) forms an acetyl derivative (VI), $C_{17}H_{24}O_5$, mp 118-120°C, $[\alpha]_D^{26}+123°$ (c 2.0; chloroform). NMR spectrum: singlet at 0.99 ppm (CH_3 at C_{10}), pair of doublets at 1.12 and 1.45 ppm (CH_3 at C_{11}), singlet at 2.00 ppm (CH_3COO), multiplet at 4.87 ppm (proton at C_6), and doublet at 5.22 ppm (H at C_4).

The hydrolysis of anhydrotetrahydroarnifolin (III) gave a substance (VII) with the composition $C_{15}H_{20}O_4$. IR spectrum, ν_{max}, cm^{-1}: 3500 (OH), 1758 (γ-lactone), 1699 and 1624 (α,β-cyclopentenone). NMR spectrum: singlet at 1.73 ppm ($CH_3-C=$), and pair of doublets at 1.12 and 1.43 ppm (CH_3-CH).

The composition, constants, and spectral characteristics of (V) correspond to dihydromexicanin C, (VI) to its acetyl derivative, and (VII) to dihydroneohelenalin, the structures of which have been reliably established previously.



All-Union Scientific-Research Institute for Medicinal Plants. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 270-272, May-June, 1971. Original article submitted February 9, 1971.

Thus, the production of (V), identical with dihydromexicanin C of known stereochemistry, permits the assumption that the full structure and stereochemistry of arnifolin are described by formula (I) [2-4].

EXPERIMENTAL

Hydrolysis of Anhydrotetrahydroarnifolin. A mixture of 1.2 g of (III) and 170 ml of 4% NaOH was heated at 60°C for 1.5 h. The substance that had not reacted was filtered off, and the filtrate was acidified with HCl to pH 1 and was treated with ether twice and then with ethyl acetate five times, and the ethyl acetate extract was washed with water to neutrality. After the elimination of the ethyl acetate, colorless crystals deposited with the composition $C_{15}H_{20}O_4$, mp 293-295.5°C (from ethyl acetate–hexane) with a yield of 0.3 g.

Hydrolysis of Dihydroanhydrotetrahydroarnifolin. In the presence of Raney Ni catalyst, 1.4 g of anhydrotetrahydroarnifolin (III) in 150 ml of ethanol was hydrogenated with the absorption of 1 mole of hydrogen. This gave 1.3 g of a faintly yellowish vitreous product (IV), which was dissolved in 20 ml of ethanol and 55 ml of 4% NaOH, the resulting solution then being heated at 60°C for 1 h. After the elimination of the ethanol and cooling, the reaction mixture was acidified with 10% HCl to pH 1. The reaction product was extracted with ether and the extract was washed with 3% $NaHCO_3$ solution and with water. After the ether had been driven off, a crystalline substance (IV), $C_{15}H_{22}O_4$, was obtained with mp 170-171.5°C (from ethyl acetate–hexane), $[\alpha]_D^{20} + 119°$ (c 2.1; chloroform).

Acetylation of the Hydrolysis Product. A mixture of 0.1 g of the substance, 2 ml of acetic anhydride, and 4 ml of pyridine was heated at 60-70°C for 1 h. The reaction product was diluted with water and extracted with ether, and the extract was washed with 5% HCl and with water. After the ether had been driven off, the product was chromatographed on silica gel. The benzene–ether (1:1) fraction gave 0.05 g of colorless crystals of (VI), $C_{17}H_{24}O_5$, mp 118-120°C (from ether), $[\alpha]_D^{26} + 123°$ (c 2; chloroform).

SUMMARY

Structure (I) is proposed for arnifolin – a sesquiterpene lactone from *Arnica foliosa* Nutt. and *Arnica montana* L.

LITERATURE CITED

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