# THE STRUCTURE OF TANAPSIN

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Continuing a study of the structure of the sesquiterpene lactone tanapsin [1], we have performed a number of chemical transformations.

The acetylation of tanapsin (I) with acetic anhydride in the presence of sulfuric acid [2] gave diacetyltanapsin (III), with the composition $C_{24}H_{32}O_8$, mp 155°C (from hexane), mol. wt. 448 (mass spectrometrically). The IR spectrum of (III) lacked the absorption bands of a hydroxy group, and the NMR spectrum showed singlets at (ppm) 0.96 (3 H, $C_{10}-CH_3$), 1.53 (3 H, $C_4-CH_3$). In the 1.75-1.90-ppm region there were signals (apart from those of the methylene protons) corresponding to two methyl groups on a double bond and to two acetoxy groups.

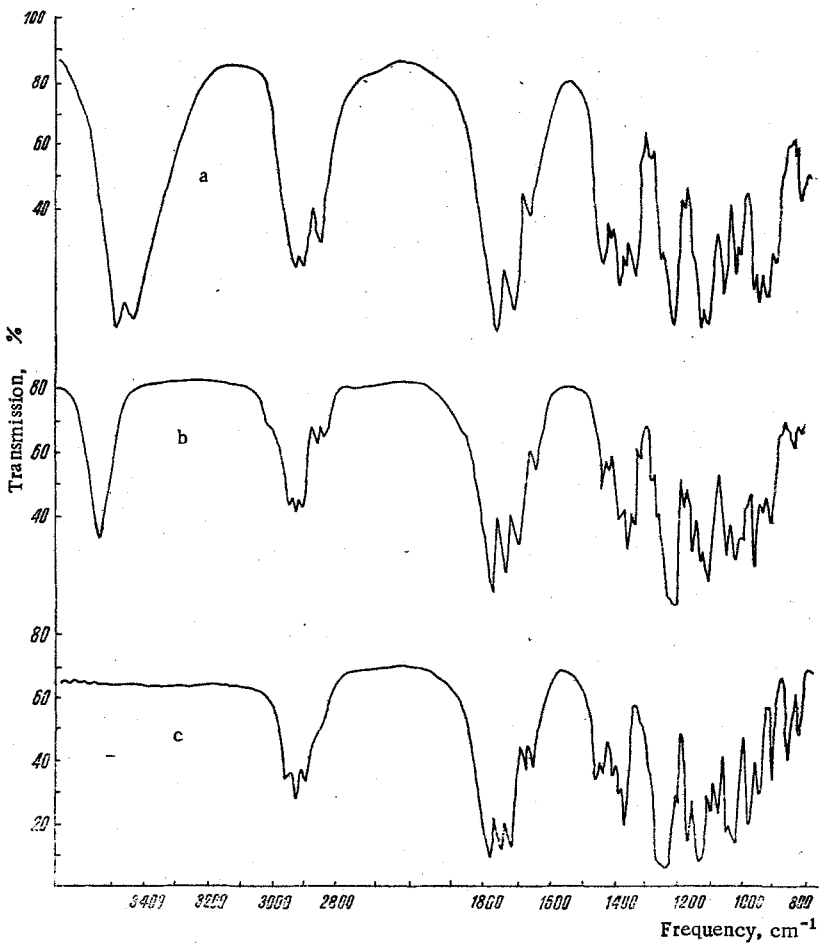


Fig. 1. IR spectra of: tanapsin (a), monoacetyltanapsin (b), and anhydromonoacetyltanapsin (c).

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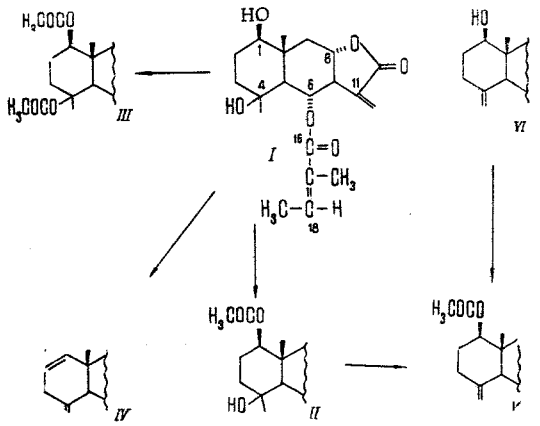
An attempt to eliminate the tertiary OH group in the lactone (I) by a literature method [3, 4] proved unsuccessful, but the dehydration of tanapsin with thionyl chloride in pyridine gave dianhydrotanapsin (IV), $C_{20}H_{24}O_4$, mp 180-181°C (from hexane), mol. wt. 328. The elimination of the hydroxy groups was confirmed by the IR spectrum. In the NMR spectrum of (IV), the signals of the protons of the tertiary hydroxyl and of the methyl group at $C_4$ had disappeared and a two-proton singlet had appeared in the 4.82-ppm region which is characteristic of an exocyclic methylene group.

The dehydration of monoacetyltanapsin (II) with thionyl chloride in the presence of pyridine gave anhydromonoacetyltanapsin (V), $C_{22}H_{28}O_6$, mp 101°C (from hexane), $M^+$ 388. The IR spectrum of (V) (Fig. 1) did not show the absorption band of hydroxy groups.

The NMR spectrum of (V) showed the following resonance signals (ppm): 0.80 (s, 3 H, $C_{10}-CH_3$), 1.79 (s, 3 H, $C_{17}-CH_3$), 1.83 (d, 3 H, $C_{18}-CH_3$), 1.90 (s, 3 H $C_1-OCOCH_3$), 4.12 (m, 1 H, $C_8-H$), 4.75 (s, 2 H, $C_4=CH_2$), 5.41 and 6.06 (d, 1 H each, $C_{11}=CH_2$).



From its melting point, a mixed melting point, and its IR spectrum substance, (V) was shown to be identical with acetylchrysanin, which we have obtained [5] from chrysanin (VI). Consequently, tanapsin has the structure of 6-angeloyloxy-1,4-dihydroxyeudesm-11(13)-en-8,12-olide.

## EXPERIMENTAL

The IR spectra (tablets with KBr) were taken on a UR-20 spectrometer, the mass spectra on an MKh-1303 mass spectrometer, and the NMR spectra on a JNM-4H-100-MHz instrument ($C_5D_5N$, $\delta$ scale, internal standard HMDS). We used Silufol for thin-layer chromatography (TLC). The solvent system was chloroform–ethanol (9 : 1) and the revealing agent 1% $KMnO_4$ in 1% $H_2SO_4$.

Isolation of the Sesquiterpene Lactones from a Chloroform Extract of Tanacetum pseudoachillea. The flower heads of the plant (50 kg) were extracted with chloroform five times, and the resin obtained was treated with 70% ethanol. The precipitate so formed was separated off, the ethanol was distilled off, and the neutral substances were extracted with chloroform. The residue after the distillation of the solvent (820 g) was separated into fractions soluble and insoluble in 30% ethanol (185 g and 615 g, respectively).

The insoluble resin (615 g) was chromatographed on a column of silica gel. Elution was performed with petroleum ether–benzene (1:1), benzene, and benzene–acetone. The petroleum ether–benzene mixture gave a 0.15% yield of tanacin calculated on the weight of the dry plant. Benzene isolated chrysanin (0.01%), and elution with benzene–acetone (9:1) gave tanapsin (0.016%), mp 191-192°C, $C_{20}H_{28}O_6$, $[\alpha]_D^{24}-139°$ (c 1.38; methanol), mol. wt. 364 (mass spectrometrically).

Monoacetyltanapsin (II). A mixture of 1 g of tanapsin with 10 ml of acetic anhydride and 10 ml of pyridine was left at room temperature for 4 h. The pyridine and the unchanged acetic anhydride were evaporated off in vacuum. The residue was chromatographed on silica gel. Elution with benzene gave 640 mg of monoacetyltanapsin with mp 127-129°C, $C_{22}H_{30}O_7$, $M^+$ 406, Rf 0.54. IR spectrum, $\nu_{max}$, $cm^{-1}$: 3530, 1775, 1735, 1705, 1660, 1240-1265, 1140.

Angelic Acid. A solution of 0.5 g of the lactone (I) in 30 ml of 4% caustic potash was heated on the water bath for 20 min. Then the mixture was cooled, diluted with water (30 ml), and acidified with 5% $H_2SO_4$ to pH 1.

The reaction product was extracted with ethyl acetate. The ethyl acetate layer was shaken with 3% sodium bicarbonate solution, and the carbonate solution was acidified and was shaken with chloroform. When the extract was concentrated, a substance crystallized out with mp 44-45°C (sublimation); it had the composition $C_5H_8O_2$ and was identified as angelic acid.

Diacetyltanapsin (III). A drop of concentrated sulfuric acid was added to a solution of 0.5 g of (I) in 20 ml of acetic anhydride, and after 10 min the mixture was diluted with water (80 ml) and was shaken with chloroform. After the solvent had been distilled off and the residue had been crystallized from hexane, 65 mg of diacetyltanapsin were obtained with mp 115°C, $C_{24}H_{32}O_8$, $R_f$ 0.7. IR spectrum, $\nu_{max}$, $cm^{-1}$: 1780, 1730, 1700, 1650, 1235-1270, 1140.

Dianhydrotanapsin (IV). A solution of 0.5 g of the lactone (I) in 5 ml of pyridine was cooled to 0°C and treated with 1 ml of thionyl chloride. After 30 min, ice was added and the mixture was shaken with chloroform.

The chloroform extracts were washed with 5% HCl and with water and were dried with sodium sulfate. The chloroform was distilled off, and the product was chromatographed on silica gel. Elution with benzene–hexane gave 90 mg of dianhydrotanapsin with mp 180-181°C, $C_{20}H_{24}O_4$, $R_f$ 0.75. IR spectrum, $\nu_{max}$, $cm^{-1}$: 1780, 1715, 1675, 1655, 1270, 1130.

Anhydromonoacetyltanapsin (V). A solution of 0.350 g of monoacetyltanapsin in 4 ml of dry pyridine was cooled to 0°C, and 0.7 ml of thionyl chloride was added. In a similar manner to the preparation of dianhydrotanapsin, benzene–hexane (3:7) eluted yielded 35 ml of anhydromonoacetyltanapsin with mp 100-101°C, $C_{22}H_{28}O_6$, $R_f$ 0.7. IR spectrum, $\nu_{max}$: 1770, 1730, 1710, 1680, 1660, 1265-1235, 1140.

Preparation of Acetylchrysanin (V) from Chrysanin (VI). A mixture of 0.110 g of chrysanin, 2 ml of acetic anhydride, and 2 ml of anhydrous pyridine was left at room temperature for 12 h and was then diluted with water. The crystals that deposited were washed with water and recrystallized from hexane. This gave 70 mg of acetylchrysanin, identical with anhydromonoacetyltanapsin.

## SUMMARY

A new eudesmanolide–tanapsin–has been isolated from the flower heads of Tanacetum pseudoachillea C. Winkl. On the basis of spectral characteristics and chemical transformations it has been established that tanapsin has the structure of 6-angeloyloxy-1,4-dihydroxyeudesm-11(13)-en-8,12-olide.

## LITERATURE CITED

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