THE STRUCTURE OF SANTACHIN

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We have reported previously that from *Achillea santolina* L., in addition to known lactones (leucomisin, austricin, and chrysartemin B) we have also isolated a lactone with the composition $C_{15}H_{18}O_4$, mp 201-202°C, $[\alpha]_D^{30}$ +10° (c 2.0; chloroform) [1], which proved not to have been described in the literature, and we have called it santachin (I).

In its melting point and chromatographic behavior, lactone I is close to leucomisin (mp 203-204°C), but it is revealed more rapidly with vanillin–sulfuric acid and its composition differs from that of leucomisin by one oxygen atom.

The UV spectrum of (I) has an absorption maximum at 236 nm (log ε 4.07), which shows the conjugation of a double bond with a carbonyl group. The IR spectrum of (I) has the absorption bands of the stretching vibrations of a γ-lactone carbonyl (1782 cm^{-1}), a ketone group (1705 cm^{-1}), and a double bond (1615 cm^{-1}).

It has been shown experimentally that the fourth oxygen atom forms an epoxide ring.

In the IR spectrum of the dihydro derivative (II) the band of the ketonic carbonyl is located at 1740 cm^{-1}. The change in the frequency of absorption of this functional group shows that in (I) there is conjugation between a double bond and a carbonyl group in a five-membered ring.

The NMR spectrum of santachin contains the signals of the protons of a secondary methyl (doublet with its center at 1.01 ppm, J = 7 Hz), of a methyl in an epoxide ring (singlet, 1.71 ppm), and of a methyl at a double bond (singlet, 2.09 ppm). These facts, and also the absence of the signal of the protons of an angular methyl group, permits us to assign santachin to the guaianolides. The signal of the lactone proton appears in the form of a triplet at 3.88 ppm ($J_{6,5}$ = 10 Hz, $J_{6,7}$ = 10 Hz) and the values of the spin–spin coupling constants indicate the β orientation of this proton. The position of the lactone ring at C_6–C_7 is confirmed by the presence of a doublet at 2.95 ppm ($J_{5,6}$ = 10 Hz). In the weak-field region there is a one-proton singlet at 6.05 ppm relating to a proton at a double bond. Under these conditions, the conjugated carbonyl group can be present only at C_2.

The presence of an epoxide group in santachin was confirmed by its cleavage with oxalic acid. The dihydroxy derivative formed has the composition $C_{15}H_{20}O_5$ (III), mp 214-215°C, M^+ 280. In the IR spectrum of (III) there is a strong broad band of hydroxy groups at 3510 cm^{-1} and also absorption bands of a lactone carbonyl (1760 cm^{-1}) and of a keto group (1700 cm^{-1}).

The PMR spectrum of (III) shows the signals of the protons of two hydroxy groups in the form of singlets at 7.84 and 6.10 ppm. There are also downfield shifts of the lactone proton

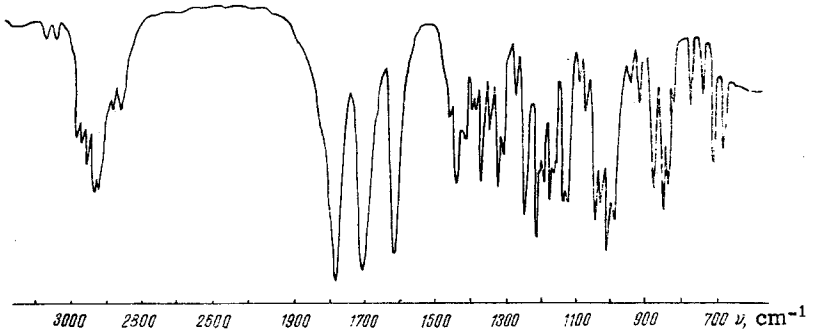

Fig. 1. IR spectrum of santachin (KBr).

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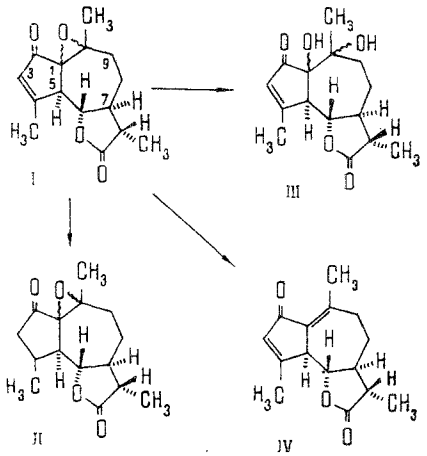
(4.75 ppm), of the C_5 proton (3.75 ppm), and of the protons of a methyl group in the geminal position to a hydroxy group (2.03 ppm).

The dihydroxy derivative of santachin is not oxidized by chromium trioxide and is not acetylated by acetic anhydride. Consequently, both hydroxyls are tertiary, and they are present at C_1 and C_{10}.

Santachin (I) was reduced with chromous chloride [2]. This gave a substance (IV) which was identified by a comparison of spectra and by a mixed melting point as leucomisin.

On the basis of the results obtained, structure (I) is suggested for santachin.



EXPERIMENTAL

The PMR spectra were taken on a JNM-4H-100/100 MHz instrument (P_y-d_5), and the chemical shifts are given in the δ scale from the signal of MHDS taken as 0. The UV spectra were recorded on an SF-4A instrument, the IR spectra on a UR-20 (KBr), and the mass spectrum on an MKh-1303. Plates with a fixed layer of silica gel and the hexane–acetone (3:1) solvent system were used for chromatographic analysis. The spots were revealed with a 1% solution of vanillin in concentrated sulfuric acid.

Isolation of Santachin (I). The air-dry comminuted epigeal part of *Achillea santolina* (40 kg) was extracted with chloroform (five times). The extract was treated with 50% ethanol (2 × 10.5 liters). The lactones were extracted from the aqueous ethanolic fraction of the extract with ether (three times: 10, 5, and 5 liters). The resin remaining after the distillation of the ether (400 g) was chromatographed on a column of silica gel (3 kg, 0.07-0.2 μ), the eluates being collected in 700-ml portions. The eluting solvents were hexane (fractions 1-10), hexane–ether (20:1) (fractions 11-21) and (8.5:1.5) (fractions 22-33), ether (fractions 34-45), and chloroform (fractions 46-60). Eluates 40-45 deposited crystls which were dissolved in chloroform and rechromatographed on silica gel. The column was washed with hexane–acetone (4:1). A mixture of two substances with R_f 0.6 was obtained. They were separated by repeated recrystallization from ethanol. Leucomisin deposited first, and the mother liquors yielded 900 mg of santachin with mp 201-202°C (ethanol).

Hydrogenation of Santachin. The hydrogenation of 50 mg of santachin dissolved in 2.5 ml of glacial acetic acid was performed in the presence of 10 mg of Adams platinum catalyst. After the absorption of hydrogen had ceased, the catalyst was filtered off, and the filtrate was diluted with water and extracted with chloroform. The solvent was evaporated in vacuum. The residue was chromatographed on silica gel with hexane–acetone (5:1). This gave the noncrystalline dihydro product with R_f 0.9.

Reaction of (I) with Oxalic Acid. A mixture of 100 mg of santachin and 10 ml of 10% oxalic acid was boiled for 1.5 h. The excess of acid was neutralized with 5% sodium bicarbonate solution. The reaction mixture was extracted with chloroform, and the solvent was evaporated in vacuum.

The residue was separated by chromatography on silica gel (20 g, 0.04-0.08 μ) with elution by hexane–acetone (4:1). This gave 60 mg of (III) with mp 214-215°C (ethanol), R_f 0.4.

Reduction of (I) with Chromous Chloride. In a current of CO_2, 3 ml of a 1 N solution of chromous chloride was added to a solution of 100 mg of santachin in 3 ml of acetic acid. The reaction was performed at 30°C for 30 min. The reaction mixture was diluted with water

and the product was extracted with methylene chloride. The residue after the elimination of the solvent in vacuum was recrystallized from ethanol. This gave a substance with mp 202-203°C identical with leucomisin (IV).

SUMMARY

1. A new guaianolide ($C_{15}H_{18}O_4$, mp 201-202°C), which had been called santachin, has been isolated from a chloroform extract of the epigeal part of *Achillea santolina* L.

2. On the basis of spectral characteristics and chemical reactions, the structure of 2-keto-1,10-epox(5,7,11-αH-6-βH)-guai-3,4-en-6,12-olide has been proposed for santachin.

LITERATURE CITED

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STRUCTURE OF UGAFERIN AND SOME PROPERTIES OF UGAMDIOL DERIVATIVES

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Continuing a study of the chemical composition of plants of the genus *Ferula*, from the roots of *Ferula ugamica* Eug. Kor, collected in the upper reaches of the river Angren in the Tashkent oblast we have isolated a new ester with the composition $C_{25}H_{36}O_7$ (M^+ 448) which we have called ugaferin (I).

The UV spectrum of (I) has a maximum at 270 nm (log ε 4.06) due to an aromatic nucleus, and the IR spectrum has absorption bands at 3400-3600 cm^{-1} (hydroxy group), 1735, 1250 cm^{-1} (ester carbonyl group), and 1615, 1560, 1520 cm^{-1} (aromatic nucleus).

When ugaferin was subjected to alkaline hydrolysis with 5% aqueous methanolic caustic potash, the neutral fraction of the hydrolysate yielded a sesquiterpene alcohol with the composition $C_{15}H_{26}O_3$ (II), mp 88-89°C, and the acidic fraction yielded an aromatic acid with the composition $C_{10}H_{12}O_5$, mp 168-169°C (III), which was identified as 3,4,5-trimethoxybenzoic acid [1]. A comparison of the physicochemical constants and spectral characteristics of the alcohol (II), the formation of a mono- and diacetate of (II) and of a mono- and diketone derivative of (II), and also the results of a study of the cyclization product of the monoacetate of (II) showed that (II) was identical with ugamdiol, isolated previously in free form from *F. ugamica* [2, 3]. The same alcohol, under the name of shiromodiol in the form of mono- and diacetates has been isolated from *Parabenzoin trilobum* [4, 5].

Thus, the proof of the structure of ugaferin reduced to determining the position of the acid residue in the ugamdiol molecule. The latter contains two secondary hydroxy groups which differ in the CS values and multiplicities of the hemihydroxylic protons in the PMR spectrum. A comparison of the PMR spectra of guamdiol and ugaferin showed that in the latter there was a downfield shift by 1.11 ppm of the signal from C_8—H in the form of a quartet. Consequently, the trimethoxybenzoic acid residue is present at C_8 and ugaferin has the structure of 8-trimethoxybenzoylugamdiol (I).

Mixed esters of ugamdiol with aliphatic and aromatic acids have been isolated from several species of *Ferula* [6, 7]. In a study of the structure of the mixed diesters of ugamdiol the main difficulty is determining the mutual positions of the acyl residues, since in this case the PMR-spectroscopic method does not always permit an unambiguous conclusion to be drawn. In view of this, we directed our attention to the fact that when the diesters of (I) are hydrolyzed with potassium carbonate in methanol at room temperature some sequence of saponification of the acid residues is observed. Thus, when the diacetate (III) and the dibenzoate (IV) of (II) are saponified under the above-mentioned conditions, the acyl residue at C_8 is split out predominantly, and the ester group at C_6 is not affected. On the other hand, the acetylation and benzoylation of ugamdiol at room temperature form, respec-

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