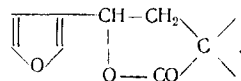


A number of bitter substances has previously [1] been isolated from *Teucrium polium* (golden germander), family Labiatae, and the structure of the main component, picropolin has been established as a diterpenoid furo lactone with a rearranged labdane carbon skeleton related to columbin [2]. In order to compare the diterpenoids of plants of this genus, we have investigated the bitter substances of the officinal species *Teucrium chamaedrys* L. (*chamaedrys* germander).

When an acetone extract of this plant was subjected to chromatographic separation on silica gel and crystallization, four new compounds with a bitter taste were isolated, which we have named respectively in order of increasing polarity *teucrins A, B, C, and D*. According to their spectral characteristics, all the substances have furan and lactone rings. The main compound – *teucin A* – according to elementary analysis and mass spectrometry is a norditerpenoid,  $C_{19}H_{26}O_6$ . Apart from a furan nucleus (1595, 1510, and  $880\text{ cm}^{-1}$ ) its molecule contains one active hydrogen atom in a hydroxy group ( $3390\text{ cm}^{-1}$ ) and two  $\gamma$ -lactone rings, one of which is  $\alpha,\beta$ -unsaturated ( $1745\text{ cm}^{-1}$ , 220 nm), while the other is saturated ( $1760\text{ cm}^{-1}$ ).

*Teucin A* undergoes no change in dilute aqueous alkali. However, in methanol containing 5–7% of alkali it dissolves readily with the absorption of two equivalents of alkali, which confirms the presence of two lactone rings in the molecule.

The hydrogenation of *teucin A* in ethanol over  $\text{Pd}/\text{BaSO}_4$  took place with the absorption of three molecular equivalents of hydrogen. The furan ring was saturated, and hydrogenolysis of one of the lactone rings took place with the formation of an acid,  $C_{19}H_{26}O_6$ , which, on standing, changed into a new lactone,  $C_{19}H_{24}O_5$ , not containing a hydroxy group. The ester oxygen of this lactone is probably in the allyl position to the furan nucleus, i.e., the *teucin* molecule has the fragment



This is confirmed by an analysis of the mass spectrum of the compound, which shows the peaks of furan-containing fragments with  $m/e$  81, 94, and 95, which are characteristic for a number of furo lactones of this type [1, 3, 4].

*Teucin B*,  $C_{20}H_{24}O_7$ , was obtained in small amount by the elution of the mixture after the separation of the main component. Its spectra show that its molecule contains a hydroxy group, a furan nucleus, and two  $\gamma$ -lactone rings ( $1770$  and  $1750\text{ cm}^{-1}$ ) and differs from *teucin A* by additional oxygen, and also by the absence from the UV spectrum of the maximum at 220 nm characteristic of an  $\alpha,\beta$ -unsaturated lactone.

The IR spectrum of *teucin C*,  $C_{20}H_{26}O_7$ , shows bands of a hydroxy group, a furan nucleus, and a  $\gamma$ -lactone ( $1750\text{ cm}^{-1}$ ) and a strong maximum at  $1725\text{ cm}^{-1}$ , which may be ascribed to a  $\delta$ -lactone. In contrast to the first two compounds, its mass spectrum has a peak with  $M-31\text{ m/e}$  which permits the assumption that a methoxy group is present in its molecule.

*Teucin D*,  $C_{19}H_{26}O_7$ , in contrast to the preceding metabolites, shows only one carbonyl maximum at  $1750\text{ cm}^{-1}$ , apparently due to a  $\gamma$ -lactone. A very strong absorption band at  $3410\text{--}3300\text{ cm}^{-1}$  and the high polarity of this compound give grounds for considering it to be a polyhydroxy derivative.

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## EXPERIMENTAL

The IR spectra were taken on a UR-10 spectrometer (KBr), the mass spectra on a MKh-1303 instrument at 145°C with an ionizing energy of 70 V, and the UV spectra on a Specord UV VIS instrument in ethanol. The melting points of the substances were determined on a Kofler block. The adsorbent for TLC was silica gel in fixed and nonfixed layers. The analyses of all the compounds corresponded to the calculated figures.

Isolation of the Teucrins. The epigeal part of the air-dry, comminuted plant collected in the flowering stage (6 kg) was exhaustively extracted with acetone at room temperature. The extract was evaporated to a volume of 800 ml and was diluted with water (2:1). The precipitate that deposited in the cold was filtered off and was washed free from waxes and chlorophyll with petroleum ether and diethyl ether and was then freed from phenols by being washed three times with a 1% aqueous solution of alkali. The residue (10 g) was chromatographed on 250 g of silica gel in chloroform. Chloroform eluted about 1 g of a mixture of phytosterols, and chloroform containing 2% methanol eluted 6.1 g of teucrin A,  $C_{19}H_{20}O_6$ , which, after three crystallizations from a mixture of acetone and ether, had mp 251-253°C,  $[\alpha]_D^{20} +19^\circ$  (c 2.8; chloroform), 163° (c 4.4; pyridine),  $R_f$  0.75 (TLC, nonfixed layer, chloroform-8% methanol system). IR spectrum,  $cm^{-1}$ : 3390, 3150, 1760, 1745, 1700, 1600, 1510, 1470, 1360, 1210, 1030, 880. UV spectrum,  $\lambda_{max}$  209, 220 nm ( $\epsilon$  10,000, 18,000). Mass spectrum (main peaks, m/e): 344  $M^+$ , 326, 297, 257, 232, 207, 188, 187, 138, 95, 94, 81.

The aqueous acetic solution was washed with petroleum ether and left to stand for two days. The precipitate that deposited, after chromatography on silica gel, yielded another 1 g of teucrin A. The mother solution was evaporated until it separated into layers and was extracted with chloroform. The extracts, consisting of a mixture of teucrins and phenolic substances, were chromatographed on silica gel. Elution with chloroform containing 2% of methanol gave an additional amount of teucrin A (0.55 g), and elution with chloroform containing 4% of methanol gave a voluminous fraction (12 g) consisting mainly of a mixture of teucrins B, C, and D. From this fraction, after repeated chromatography with different ratios of adsorbent and substance, careful selection of the fractions, and a gradual change in the concentration of methanol in chloroform from 3 to 5% (checked by TLC), all three substances were isolated in the pure state, with  $R_f$  0.50, 0.45, and 0.40, respectively (under the conditions for the chromatography of teucrin A).

Teucrin B. Composition  $C_{20}H_{24}O_7$  (0.5 g), mp 239-241°C (from acetone-ether). IR spectrum,  $cm^{-1}$ : 3510, 3420, 3150, 3160, 1770, 1750, 1600, 1510, 880. UV spectrum:  $\lambda_{max}$  212 nm ( $\epsilon$  7000).

Teucrin C. Composition  $C_{20}H_{26}O_7$  (0.4 g), mp 191-193°C (from a mixture of acetone and ether). IR spectrum,  $cm^{-1}$ : 3470, 3400, 3290, 3150, 1750, 1725, 1590, 1503, 880. UV spectrum:  $\lambda_{max}$  212 nm ( $\epsilon$  7000).

Teucrin D. Composition  $C_{19}H_{26}O_7$  (1.5 g), mp 220-222°C (from a mixture of methanol and chloroform),  $[\alpha]_D^{20} +19^\circ$  (c 4.4; pyridine). IR spectrum,  $cm^{-1}$ : 3410-3300, 1750, 1590, 1505, 880. UV spectrum:  $\lambda_{max}$  212 nm ( $\epsilon$  6600).

Hydrogenation of Teucrin A. The saturation of 350 mg of teucrin in 20 ml of ethanol with hydrogen was performed in the presence of 70 mg of 4% of Pd/BaSO<sub>4</sub>. Over 6 h at 25°C and 755 mm, 80 ml of hydrogen was absorbed, which corresponds to 2.9 equivalents. The residue after the separation of the catalyst and the evaporation of the solvent was dissolved in chloroform, and the solution was washed with 5% sodium carbonate solution to remove the acid fraction. The chloroform, containing the neutral product, was washed with water, dried with sodium sulfate, and distilled. This gave 80 mg of a lactone  $C_{19}H_{24}O_5$ , mp 187-189°C (from chloroform-ether),  $[\alpha]_D^{20} +225^\circ$  (c 5.6; chloroform). IR spectrum (in chloroform),  $cm^{-1}$ : 1780, 1755, 1690, 1455, 1365. UV spectrum:  $\lambda_{max}$  219.5 nm ( $\epsilon$  14,500).

The carbonate solution was carefully acidified with dilute hydrochloric acid to pH 7. The precipitate that deposited was dissolved in chloroform, and the solution was washed with water, dried with sodium sulfate, and distilled.

The residue (260 mg) was methylated with diazomethane in a mixture of methanol and ether. After the usual working up, 260 mg of an amorphous substance was obtained. IR spectrum (in chloroform),  $cm^{-1}$ : 3400, 1755, 1705, 1240. After some days, this methyl ester had changed into a crystalline product identical with the lactone described above.

## SUMMARY

The plant Teucrium chamaedrys, family Labiatae, has yielded four new bitter principles which have been characterized and named teucrins A, B, C, and D. According to preliminary results, these compounds belong to the norditerpene furo lactone group.

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