THE STEREOCHEMISTRY OF STACHYSOLONE

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The structure of stachysolone – a diterpenoid from Stachys annua L. – has been shown previously [1]. On the basis of spectral and chemical data it was established that stachysolone belongs to the diterpenoids with a rearranged labdane carbon skeleton and is represented by formula (I), without taking the spatial arrangement into account. We have now studied the stereochemistry of this compound.

Among diterpenoids with a rearranged labdane skeleton, compounds are known with the trans [2, 3] and cis [4] linkages of the A/B rings. In order to determine to which series stachysolone belongs, we decided to correlate it with the known ketone (II) obtained [5] from plathyterpol, for which the cis (5β) linkage of the rings has been established [4]. However, after stachysolone had been oxidized with the Jones reagent to the triketone (III), this had been reduced by the Wolff–Kishner method to the hydrocarbon (IV), and the latter had been oxidized with sodium dichromate in acetic acid, the α,β-unsaturated ketone (V) was obtained, which differed from compound (II) in its melting point and optical properties.

The circular dichroism curve of the ketone (V) (Fig. 1) corresponds completely in the sign of the Cotton effect (CE) and in the fine structure of the R band to that described in the literature [6, 7] as characteristics for Δ^1-5α-3-oxosteroids (and also Δ^3-5α-2-oxosteroids) and differs sharply from that of the Δ^1-5β-isomers. This gave grounds for assuming that compound (V), unlike (II), belongs to the trans series and, consequently, the carbon skeletons of plathyterpol and stachysolone likewise differ by the configuration at C_5. A final conclusion was drawn after a comparison of the optical rotatory dispersion (ORD) curves of stachysolone and tetrahydrostachysolone (Fig. 2) with the curves given in the literature for derivatives of trans- and cis-decalins and of some steroids and terpenes with a known stereochemistry. Thus, the ORD curve of stachysolone is very similar in shape, in the sign of the CE, and in the position of the extrema

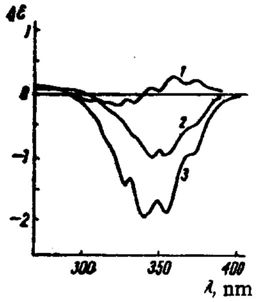

Fig. 1

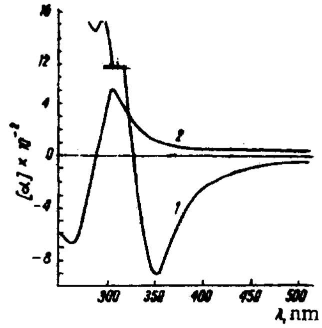

Fig. 2

Fig. 1. Circular dichroism curves: 1) 17β-hydroxy-5β-androst-1-en-3-one acetate; 2) 17β-hydroxy-5α-androst-1-en-3-one; 3) the ketone (V).

Fig. 2. ORD curves: 1) stachysolone; 2) tetrahydrostachysolone.

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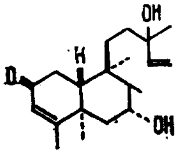
to the curve of (−)-trans-9-methyl-3-oxo-2,3,4,5,7,8-hexahydronaphthalene [8] and has the opposite sign of the CE to the curve of (+)-Δ^1-trans-methyloctal-3-one [9].

Tetrahydrostachysolone has a CE of the opposite sign to stachysolone, as is the case for the products of the hydrogenation of the trans-hexahydronaphthalenes [8, 10]. The ORD curve of tetrahydrostachysolone is very similar in shape and sign of the CE to the curves of cholestan-3-one [11], cholestan-2-one [12], α-tetrahydrosantonin [13] and other trans (5α,10β) 2-oxo derivatives and is opposite to the sign of compounds with the reversed stereochemistry at the centers such as, for example, trans-10α-methyldecal-2-one [13]. This gives grounds for regarding stachysolone as a derivative of a rearranged labdane of the type of kolavane with the trans (5α,10β) linkage of the A/B rings.

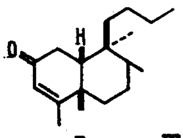
The configuration at C_7 becomes clear from a study of the NMR spectrum [1]. The half-width of the H_7 signal is 9 Hz, which shows the equatorial orientation of the proton and, consequently, the hydroxyl is present in the axial position. This is also confirmed by the difficulty of its acetylation, which takes place only on heating.

The side chain at C_9 must be present, as in all bicyclic diterpenoids, in the most energetically favorable equatorial position. The configuration at the C_8 and C_{13} atoms is still undetermined, and will be discussed separately.

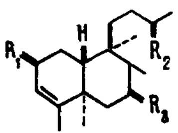
Thus, when the configurations of four of the asymmetric centers out of the six are considered, stachysolone can be represented by formula (I).



I



II



III. $R_1=R_2=R_3=O$ IV. $R_1=R_2=R_3=H_2$.
V. $R_1=O$, $R_2=R_3=H_2$

EXPERIMENTAL

The IR spectra were taken on a UR-10 spectrometer. The ORD curves were determined on a Jasco ORD/UV-5 spectropolarimeter at 27°C. The circular dichroism curves were obtained on a Spectropol B instrument by V. A. Babkin (Institute of Organic Chemistry, Novosibirsk). The melting points were measured on a Kofler block.

Stachysolone. ORD: $[\alpha]_D$ −25°, $[\alpha]_{450}$ −99°, $[\alpha]_{390}$ −277°, $[\alpha]_{352}$ −915°, $[\alpha]_{330}$ −199°, $[\alpha]_{298}$ + 1542°, $[\alpha]_{285}$ + 1472° (c 0.119; methanol).

Tetrahydrostachysolone. ORD: $[\alpha]_D$ + 15°, $[\alpha]_{450}$ + 22°, $[\alpha]_{360}$ + 79°, $[\alpha]_{330}$ + 193°, $[\alpha]_{305}$ + 508°, $[\alpha]_{264}$−700°, $[\alpha]_{250}$−607° (c 0.28; methanol).

Oxidation of Stachysolone. With stirring at 0°C, the Jones reagent [14] was added dropwise to 500 mg of the substance in 10 ml of acetone until a brown color persisting for 30 min appeared. Then the mixture was diluted with water and extracted with chloroform, and the extract was washed with a 2% solution of alkali and with water, and dried, and the chloroform was distilled off. The residue was chromatographed on alumina (activity grade III). A mixture of benzene and 5% of ethanol eluted 300 mg of the triketone (III), mp 145-146°C (from petroleum ether−benzene). IR spectrum (KBr), cm^{-1}: 1710, 1660, 1620, 845.

Found %: C 74.37, 74.39; H 8.95; 8.93 · $C_{18}H_{26}O_3$. Calculated %: C 74.44; H 9.03.

Wolff−Kishner Reduction of the Ketone (III). To 150 mg of compound (III) were added 15 ml of diethyleneglycol and 4 ml of 85% hydrazine hydrate. The mixture was heated at 125°C for 3 h, and then the temperature was raised to 210°C and 200 mg of KOH was added. Heating was continued at 245°C for 8 h. Then the mixture was poured into water and extracted with ether. The residue (100 mg) was chromatographed on 6 g of alumina. Petroleum ether eluted 50 mg of the hydrocarbon (IV).

Found %: C 87.22, 87.17; H 12.88, 12.96. Mol. wt. 248 (mass spectrum): $C_{18}H_{32}$. Calculated %: C 87.01; H 12.98. Mol. wt. 248.44.

Oxidation of the Hydrocarbon (IV) with Sodium Dichromate. To a cooled solution of 50 mg of the substance in a mixture of benzene and acetic acid was added a saturated solution of 60 mg of sodium dichromate in acetic acid. The mixture was left at 0°C for 24 h. Then it was diluted with water and extracted with ether, the extract was washed with sodium bicarbonate solution and with water and was dried, and the ether was distilled off. The residue was chromatographed on alumina. A mixture of petroleum ether and benzene (1 : 1) eluted 20 mg of a crystalline substance with mp 110-112°C (from petroleum ether). IR spectrum (KBr), cm^{-1}: 1660 (α,β-unsaturated ketone), 1620, 850 (double bond). UV spectrum (in ethanol): 240 nm (ε 11,000). Circular dichroism, λ_{nm} (Δε): 400 (−0.12), 385 (−0.14), 371 (−0.94), 365 (−0.82), 354 (−1.88), 347 (−1.59), 340 (−1.98), 331 (−1.30), 328 (−1.45), 318 (−0.77), 315 (−0.75), 305 (−0.27), 290 (0), 267 (+ 0.09) (c 0.096; heptane).

Found %: C 82.32, 82.05, H 11.61, 11.50. Mol. wt. 262 (mass spectrum). $C_{18}H_{30}O$. Calculated %: C 82.38; H 11.52. Mol. wt. 262.42

SUMMARY

The configurations of four of the six asymmetric centers of stachysolone have been established. This diterpenoid belongs to compounds with the trans (5α,10β) linkage of the A/B rings.

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