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DITERPENOIDS FROM STACHYS ANNUA

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Continuing a study of the substances from plants of the family Labiatae [1, 2], we have investigated compounds isolated from Stachys annua L. (hedgenettle betony).

Chromatographic separation on alumina of an acetone extract of the plant collected in the flowering stage in the steppe regions of Moldavia gave three new diterpene compounds: a diacetate $C_{24}H_{36}O_5$ and two isomeric monoacetates $C_{22}H_{34}O_4$ denoted in the order of elution from the column by A and B.

Saponification of these esters with methanolic alkali gave the new bicyclic diterpene ketodiol $C_{20}H_{32}O_3$, bitter to the taste, which we have called stachysolone.

The IR and UV spectra of stachysolone showed that it contains hydroxy and keto groups and also two double bonds, one of which is a vinyl bond and the other a trisubstituted double bond conjugated with a carbonyl group. The presence of two active hydrogen atoms in stachysolone shows that its molecule contains two hydroxy groups. Hydrogenation of the diterpenoid in ethyl acetate over a palladium catalyst gave tetrahydrostachysolone $C_{20}H_{36}O_3$, readily forming a thiaketal with mercaptan.

Acetylation of stachysolone over acetic anhydride took place only on heating to 70° C; the compound yielded a mixture of three acetates which were identical with the native products. The action on stachysolone of chromic anhydride in pyridine oxidized only one hydroxy group, forming oxostachysolone, $C_{20}H_{30}O_3$.

The diacetate and monoacetate B are not oxidized by chromic anhydride, while the monoacetate A is converted on oxidation into the ketone $C_{22}H_{32}O_4$. This shows that stachysolone contains secondary and tertiary hydroxy groups, and the monoacetates A and B differ only in the position of the acetyl group.

Experimental

Melting points were determined on a Kofler block, the IR spectra were taken on a UR-10 spectrometer and the UV spectra on an SF-4 instrument, the molecular weights were measured mass-spectrometrically, and the $[\alpha]_D$ values were determined in chloroform.

Isolation of the stachysolone acetates. Eight kilograms of the dry plant was exhaustively extracted with acetone, giving 190 g of total extract. The plant waxes were eliminated by precipitation from methanol. The residue (69 g) was dissolved in ether and the solution was washed with 10% alkali. The neutral product (31 g) was chromatographed on 800 g of alumina (activity grade III). The substances were eluted from the column successively with petroleum ether, benzene, diethyl ether, and methanol.

The ethereal fraction (10 g) was rechromatographed on 500 g of alumina (activity grade III). A mixture of benzene and 10% of ether eluted 4.4 g of stachysolone diacetate. Crystallization from petroleum ether containing 10% of diethyl ether yielded crystals with mp 91-92° C, $[\alpha]^{20}_{D}$ $-71.2°$ (c 7.7). IR spectrum (CCl_4): 1738 cm^{-1} and 1240 cm^{-1} (acetate), 1675 cm^{-1} (α,β-unsaturated ketone), and 1620, 925, and 850 cm^{-1} (double bonds). Found, %: C 71.42; 71.49; H 9.02; 9.06; mol. wt. 404. Calculated for $C_{24}H_{36}O_5$, %: C 71.25; H 8.97; mol. wt. 404.53.

Elution with a mixture of benzene and 15% of diethyl ether yielded the monoacetate A. After crystallization from a mixture of petroleum ether and benzene it had mp 134-136° C, $[\alpha]^{20}_{D}$ $-47.6°$ (c 7.4). IR spectrum ($CHCl_3$): 3620 and 3490 cm^{-1} (hydroxyl), 1730 and 1250 cm^{-1} (acetate), 1670 cm^{-1} (α,β-unsaturated ketone), and 1620, 925, and 850 cm^{-1} (double bonds). Found, %: C 72.98; 73.21; H 9.51; 9.48; mol. wt. 362. Calculated for $C_{22}H_{34}O_4$, %: C 72.89; H 9.45; mol. wt. 362.49.

The monoacetate B was eluted with a mixture of benzene and 40% of diethyl ether. After crystallization from petroleum ether with the addition of benzene it had mp 154-155.5° C, $[\alpha]^{20}_{D}$ $-77°$ (c 7.2). IR spectrum ($CHCl_3$): 3600 and 3450 cm^{-1} (hydroxyl), 1730 and 1250 cm^{-1} (acetate), 1665 cm^{-1} (α,β-unsaturated ketone), and 1620, 930, and 850 cm^{-1} (double bonds). Found, %: C 73.11; 73.02; H 9.46; 9.55; mol. wt. 362. Calculated for $C_{22}H_{34}O_4$, %: C 72.89; H 9.45; mol. wt. 362.49.

Saponification of stachysolone diacetate. A solution of 1 g of the diacetate in 20 ml of methanol containing 10% of caustic potash was heated for 2 hr. The methanol was distilled off, water was added, and the mixture was extracted with ether. The ethereal solutions were washed with water to neutrality and were dried with sodium sulfate, and the ether was distilled off. The residue was crystallized from a mixture of methylene chloride and petroleum ether to give

0.75 g of stachysolone with mp 153–155° C. A mixture with the monoacetate B melted at 125–130° C, $[\alpha]^{20}_{D}$ −54.6° (c 6.99). UV spectrum: λ_{max} (in ethanol) 239 mμ (log ε 4.05). IR spectrum ($CHCl_3$): 3160 and 3480 cm^{-1} (hydroxyls), 1665 cm^{-1} (α,β-unsaturated ketone), and 1620, 928, and 850 cm^{-1} (double bonds). Found, %: C 74.85; 74.86; H 10.08; 10.01; H_{act} 0.64; mol. wt. 320. Calculated for $C_{20}H_{32}O_3$, %: C 74.96; H 10.06; $2H_{act}$ 0.62; mol. wt. 320.46.

Saponification of the monoacetates. The monoacetates A and B were saponified as described above. This gave crystalline substances identical with stachysolone with respect to thin-layer chromatography, melting points, mixed melting points, and IR and UV spectra.

Hydrogenation of stachysolone. A solution of 580 mg of stachysolone in 20 ml of ethyl acetate was saturated with hydrogen in the presence of 5% $Pd/SrCO_3$. At 20° C and 750 mm, 84 ml of hydrogen was absorbed, which corresponds to 1.9 equivalents. After the usual treatment, 570 mg of tetrahydrostachysolone was obtained with mp 150–151° C (from ethyl acetate), $[\alpha]^{20}_{D}$ +15.1° (c 11.9). IR spectrum ($CHCl_3$): 3620 and 3450 cm^{-1} (hydroxyl), and 1707 cm^{-1} (ketone). Found, %: C 74.32; 74.20; H 11.33; 11.05; mol. wt. 324. Calculated for $C_{20}H_{36}O_3$, %: C 74.02, H 11.19; mol. wt. 324.49.

To 250 mg of tetrahydrostachysolone in 1.5 ml of glacial acetic acid were added 100 mg of ethanedithiol and two drops of boron trifluoride etherate, and the solution was left at 0 to +5° C for 2 hr. After dilution with water, the thioketal was extracted with ether and the ethereal extracts were washed with alkaline solution and with water, dried with sodium sulfate, and distilled. The residue was crystallized from a mixture of methylene chloride and petroleum ether; mp 146–148° C. Found, %: C 66.58; H 10.20; 16.14; mol. wt. 400. Calculated for $C_{22}H_{40}O_2$, %: C 65.92; H 10.06; 16.01; mol. wt. 400.86.

Oxidation of stachysolone. A solution of 70 mg of stachysolone in 1.5 ml of pyridine was added to the complex obtained from 100 mg of chromic anhydride and 1 ml of anhydrous pyridine, and the mixture was left for 2 hr at room temperature. After the usual treatment, 50 mg of oxostachysolone with mp 176–177.5° C (from a mixture of petroleum ether and methylene chloride) was obtained. IR spectrum ($CHCl_3$): 3610 and 3460 cm^{-1} (hydroxyl), 1710 cm^{-1} (ketone), 1 1665 cm^{-1}(α,β-unsaturated ketone), and 1620, 928, and 855 cm^{-1} (double bonds). Found, %: C 75.78; 75.50; H 9.49; 9.56. Calculated for $C_{20}H_{30}O_3$, %: C 75.43; H 9.50.

Oxidation of the monoacetate A. Sixty milligrams of the monoacetate was oxidized with chromic anhydride in pyridine as described for stachysolone. After chromatography on 3 g of silica gel, 50 mg of the liquid monoacetate of oxostachysolone was obtained. IR spectrum (film): 3380 cm^{-1} (hydroxyl), 1738 and 1248 cm^{-1} (acetate), 1710 cm^{-1} (ketone), 1670 cm^{-1} (α,β-unsaturated ketone), and 1620 cm^{-1} (double bond).

Oxidation of the monoacetate B. One hundred milligrams of the monoacetate was oxidized under the condition described above. Working up yielded 95 mg of a substance the IR spectra and melting point of which were identical with those of the initial monoacetate. A mixture gave no depression of the melting point.

After the action of the oxidizing agent on the monoacetate for 24 hr, it again remained unchanged.

Acetylation of stachysolone. A mixture of 200 mg of stachysolone, 5 ml of anhydrous pyridine, and 4 ml of acetic anydride was heated in a flask with a reflux condenser at 70° C for 5 hr. Then it was poured into cold water and extracted with ether, and the ethereal solution was washed with sodium bicarbonate solution, dilute hydrochloric acid, and water; dried with sodium sulfate; and distilled. The residue was chromatographed on 10 g of alumina (activity grade III). A mixture of petroleum ether and 20% of benzene eluted 10 mg of a low-polarity liquid containing no hydroxy groups; petroleum ether–benzene (1 : 1) eluted 25 mg of stachysolone diacetate, mp 91–92° C. A mixture of benzene and 5% of ether eluted, first, 60 mg of the monoacetate A, mp 134–136° C, and then 15 mg of a mixture of the monoacetates A and B, and 70 mg of the monoacetate B, mp 154–155° C. From the IR spectra, behavior on thin-layer chromatography, and the absence of depressions of the melting points of mixed samples, these esters were shown to be identical with the corresponding natural acetates. Benzene containing 10% of ether eluted 15 mg of unchanged stachysolone.

Conclusions

From Stachys annua L. have been isolated the diacetate and two monoacetates of a new diterpenoid $C_{20}H_{32}O_3$, which has been named stachysolone. It has been shown that stachysolone is a bicyclic α,β-unsaturated ketone containing secondary and tertiary hydroxy groups.

REFERENCES

1. L. A. Salei, D. P. Popa, and G. V. Lazur'evskii, KhPS [Chemistry of Natural Compounds], 2, 249, 1966.
2. D. P. Popa, G. S. Pasechnik, and Fang Tkhuk An, KhPS [Chemistry of Natural Compounds], 4, 345, 1968.

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