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STRUCTURE OF KARATAVICIN

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From the roots of Ferula karatavica Rgl. et Schmalh., collected in the region of Chengel'dy, Kazakh SSSR, we have isolated a substance with the composition $C_{24}H_{30}O_5$ (previously [1] the substance was given the empirical composition $C_{21}H_{28}O_4$), which we have called karatavicin [1]. The UV and IR spectra (Fig. 1) show that karatavicin is a coumarin compound. This is confirmed by the production of umbelliferone by its acid hydrolysis.

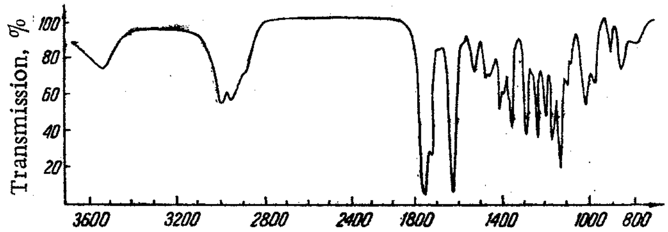


Fig. 1. IR spectrum of karatavicin in carbon tetrachloride.

In addition to a lactone ring (band at 1750 cm^{-1}) and an ether linkage, karatavicin has one tertiary OH group (band at 3520 cm^{-1}) and one CO group (band at 1718 cm^{-1}). Although the OH group is tertiary (shown by the fact that karatavicin cannot be oxidized with chromic anhydride), the substance obtained forms a monoacetate with the composition $C_{26}H_{32}O_6$, which, like karatavicin itself, is optically inactive.

The presence of a CO group was shown definitely by exhaustive hydrogenation of karatavicin in glacial acetic acid with platinum oxide, when it was split at the position of the ether link to give two fragments: umbelliferone and a saturated liquid ketol with the composition $C_{15}H_{30}O_2$, the UV spectrum of which exhibited an absorption maximum at 274 mμ (log ε 1.63) which is characteristic for a nonconjugated ketone, while the IR spectrum had a band at 1713 cm^{-1} (CO group in a saturated aliphatic chain).

The presence of an OH group is confirmed by a strong maximum at 3490 cm^{-1}.

On reduction with lithium aluminum hydride, the ketol was readily converted into a diol. The IR spectrum of the latter lacked the band at 1713 cm^{-1} and the band in the 3400 cm^{-1} region had become broader because of the superposition of the two hydroxyl bands.

Oxidation of the diol with chromic anhydride re-formed the original ketol.

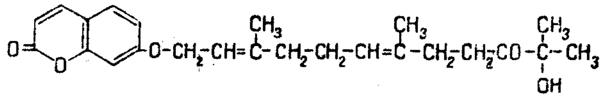
When the ketol was reduced by Clemensen's method, a hydrocarbon was obtained with physical constants and an IR spectrum identical with those of farnesane. These results permit the assumption that the aliphatic chain of karatavicin is of the farnesol type.

In view of the empirical composition of karatavicin and the presence of one CO group in it, we have assumed that its aliphatic chain contains not three but two double bonds, which, judging from the IR spectrum, are not conjugated with one another, or with the CO group. To determine the position of the double bonds, karatavicin was ozonized.

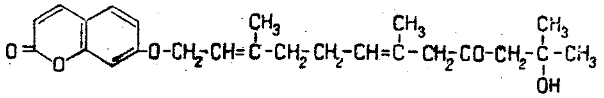
The ozonation products were found to contain levulinic aldehyde [2], while no formaldehyde, formic acid, acetone, acetone peroxide, acetaldehyde, or acetic acid was found, which shows that karatavicin has no isopropylidene grouping and does have double bonds adjacent to CH_3 groups, as has been established for farnesol.

On the basis of these results, we assign to karatavicin the two possible structural formulae (I) and (II), which also do not contradict the NMR spectrum (Fig. 2):

I



II



The position of the tertiary hydroxyl shown in the formulae is confirmed by a singlet signal with τ 8.64. The two triplets (τ 4.85 and τ 4.55) present apparently correspond to the two vinyl protons. The signals with τ 8.38 and τ 8.26 can be ascribed to the vinyl methyl protons. In our opinion, formula (I) is preferable.

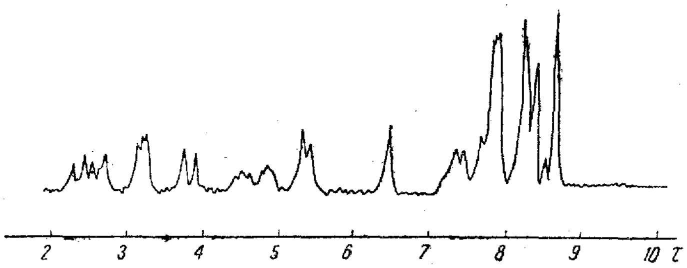


Fig. 2. NMR spectrum of karatavicin in carbon tetrachloride.

Experimental

Isolation of karatavicin. Forty grams of the neutral fraction of the resin of the roots of Ferula karatavica was dissolved in a small amount of chloroform and chromatographed on a column (800 g of Al_2O_3 with activity grade III). It was eluted with a mixture of petroleum ether and chloroform (1:7).

The viscous oil was crystallized from petroleum ether–diethyl ether (1:3). This gave karatavicin with mp 59–60° C, R_f 0.23 (Al_2O_3, activity grade III, chloroform). UV spectrum: 322 and 222 mμ (log ε 4.10, 3.78, respectively); IR spectrum: 3520, 1750, 1718, 1620, 1518, 1408 cm^{-1}.

Found, %: C 72.20, 72.15; H 7.70, 7.61. Calculated for $C_{24}H_{30}O_5$, %: C 72.36; H 7.53.

Karatavicin underwent no change on treatment with chromic anhydride in acetone solution.

Acid degradation of karatavicin. A solution of 0.6 g of the substance in 10 ml of glacial acetic acid was treated with five drops of concentrated sulfuric acid and heated in the water bath for 1 hr. Then the mixture was diluted with water and the umbelliferone was extracted with ether. This material gave no depression of the melting point in admixture with authentic umbelliferone (mp 228–230° C from water), and their IR spectra were also identical.

Karatavicin monoacetate. One gram of karatavicin in 6 ml of a mixture of pyridine and acetic anhydride (1:1) was heated in the water bath for 7–8 hr. The solvent was distilled off and the residue was recrystallized from petroleum ether–diethyl ether (1:3). The melting point of the monoacetate was 71–72° C; R_f 0.58 (Al_2O_3, activity grade III; chloroform). UV spectrum: 322, 222 mμ (log ε 4.22, 4.69, respectively). IR spectrum: 1740, 1620, 1560, 1512, 1408, 1260 cm^{-1}.

Found, %: C 71.14, 71.28; H 7.58, 7.69. Calculated for $C_{26}H_{32}O_6$, %: C 70.90; H 7.27.

Saponification of the monoacetate gave the initial karatavicin.

Hydrogenation of karatavicin. Five grams of karatavicin in 30 ml of glacial acetic acid was hydrogenated in the presence of 0.5 g of platinum oxide. It absorbed 1406 ml of hydrogen. A chloroform extract was washed with water, evaporated to small bulk, and chromatographed on a column Al_2O_3, activity grade III. It was eluted with chloroform–petroleum ether (1:5). This gave a liquid ketol with n_D^{20} 1.4470, R_f 0.58 (Al_2O_3, activity grade III, chloroform). UV spectrum: 274 mμ (log ε 1.63). IR spectrum: 3490 (OH group and 1713 cm^{-1} (CO group of a ketol).

Found, %: C 74.00, 73.94; H 12.51, 12.56. Calculated for $C_{15}H_{30}O_2$, %: C 74.38; H 12.39.

On oxidation with chromic anhydride in acetone solution, the ketol underwent no change. On further extraction with chloroform, umbelliferone was isolated from the hydrogenation products and identified.

Reduction of the ketol. To 0.3 g of the ketol in 20 ml of absolute ether was added 0.3 of lithium aluminum hydride, and the mixture was left for 24 hr. Then moist ether and a saturated aqueous solution of sodium sulfate were added. The ethereal layer was separated off, dried with sodium sulfate, and distilled. This gave a liquid, apparently a diol, with n_D^{20} 1.4570, R_f 0.10 (Al_2O_3, activity grade III, chloroform). The IR spectrum had no band of a CO group and had a maximum in the OH group region at 3420 cm^{-1} (broad).

Found, %: C 73.40, 73.41; H 13.18, 13.16. Calculated for $C_{15}H_{32}O_2$, %: C 73.77; H 13.11.

Reduction of the ketol by Clemmensen's method. A mixture of concentrated hydrochloric and acetic acids (3:7), followed by 1 g of the ketol in 30 ml of acetic acid, was added to amalgamated zinc. After 48 hr, the mixture was heated in the water bath for 1 hr and was then shaken with petroleum ether and filtered through a 15-cm layer of alumina (activity grade II), after which the solvent was distilled off. This gave a hydrocarbon with n_D^{20} 1.4364, d_4^{20} 0.7746 having the composition $C_{15}H_{32}$ and an IR spectrum identical with that of farnesane.

Ozonization of karatavicin. At −10° C, ozone was passed through a solution of 3 g of karatavicin in 20 ml of chloroform until a 10% aqueous solution of potassium iodide became intensely colored. The chloroform was distilled off in vacuum. The residue—a viscous yellowish liquid—was heated in the boiling water bath with 100 ml of water under reflux for 2 hr. Then 20 ml of liquid was distilled off, and 5 ml of a saturated aqueous solution of phenylhydrazine hydrochloride and 1 ml of concentrated hydrochloric acid was added to it. Methylphenyldihydropyridazine was isolated with mp 195–196° C (from ethanol) this being characteristic for the corresponding derivative of levulinic aldehyde. It gave one spot with R_f 0.90 (Al_2O_3, activity grade III, chloroform).

The microanalyses were performed by E. A. Sokolova, the IR spectra were taken on a UR-10 instrument by T. V. Bukreeva, and the NMR spectrum of karatavicin was recorded and interpreted by V. I. Sheichenko.

Summary

From the neutral fraction of the resin of the roots of Ferula karatavica Rgl. et Schmalh. an optically inactive coumarin, karatavicin, $C_{24}H_{30}O_5$, has been isolated; it is an ether of umbelliferone and a sesquiterpene aliphatic ketodiol. Two possible structural formulae (I) and (II) have been proposed for karatavicin.

REFERENCES

1. N. P. Kir'yalov, Trudy BIN AN, seriya V, Rastitel'noe syr'e, no. 12, 90, 1965.
2. N. P. Kir'yalov, Trudy BIN AN, seriya V, no. 8, 7, 1961.

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