UDC 577.15/17:582.89

THE STRUCTURE OF KARATAVIC ACID

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Khimiya Prirodnykh Soedinenii, Vol. 4, No. 5, pp. 283-287, 1968

Karatavic acid was first obtained by V. P. Bersutskii [1]. It was later studied by N. P. Kir'yalov [2]. However, the structure of the acid was not determined.

The acid, $C_{24}H_{28}O_5$, mp 89-90° C, forms methyl and ethyl esters ($C_{25}H_{30}O_5$ with mp 106-107° C and $C_{26}H_{32}O_5$ with mp 124-125° C, respectively). Both the acid itself and its esters are readily decomposed by the action of mineral acids with the formation of umbelliferone.

The IR spectrum (Fig. 1) of the acid confirms its coumarin nature.

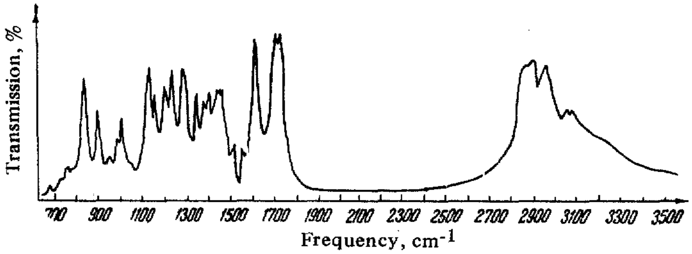


Fig. 1. IR spectrum of karatavic acid in paraffin oil.

Valuable information for the determination of the structure of karatavic acid was obtained by a study of the NMR spectra of the acid and its esters and their hydrogenated derivatives.

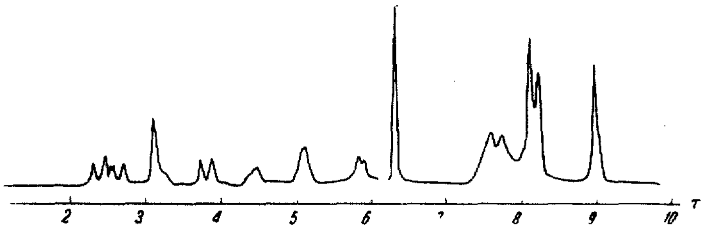


Fig. 2. NMR spectrum of methyl karatavate in carbon tetrachloride at 20° C and a frequency of 60 MHz.

Thus, the NMR spectrum of the methyl ester of the acid under consideration (Fig. 2) was interpreted in the following way: the singlet signal with τ 9.0 (3H) corresponds to a tertiary methyl group. A vinylmethyl group and three methylene groups apparently absorb in the region τ 7.9-8.3 (9H). Three methylene groups also absorb in the region τ 7.3-7.9 (6H). The signal at τ 6.35 (3H) represents the protons of a methyl group in an ester; τ 5.85 (1H) the proton of a methine group on an ether bond; τ 5.1 (2H) an exocyclic methylene group, and τ 4.45 (1H) a vinyl proton. The protons of a coumarin nucleus resonate in the region τ 2.2-3.9.

An analysis of the NMR spectrum showed that in karatavic acid the umbelliferone is linked by an ether bond to a hydroxy acid with a monocyclic structure possibly having two nonconjugated double bonds, one of which is exocyclic. We were able to confirm the presence of the latter by the fact that ozonization of the ethyl karatavate gave formaldehyde.

The exhaustive hydrogenation of ethyl karatavate in solution in acetic acid in the presence of platinum oxide followed by the chromatographic separation of the hydrogenation products yielded a liquid ethyl ester of a hydroxy acid of the composition $C_{17}H_{32}O_3$, the saponification of which furnished the hydroxy acid $C_{15}H_{28}O_3$ with mp 143-144° C, $[\alpha]_D$ $-20.25°$ (c 3.16; ethanol), its hydroxy group being secondary. However, this hydroxy acid proved to be unknown.

In its mass spectrum (Fig. 3) there was no corresponding molecular ion. This is due to the fact that the ionized molecule loses a molecule of water and forms an ion with mass 238 m/e.

In view of the results of the interpretation of the NMR spectrum of methyl karatavate (and no other NMR spectra of this series have so far been published) and the results obtained on the hydrogenation of the saturated hydroxy acid $C_{15}H_{28}O_3$, we assumed that the nonumbelliferone moiety of the molecule of karatavic acid possesses the carbon skeleton of humulane or one similar to it. One of the two most probable structures is formulated as (I) or (II).

However, we have not yet succeeded in isolating humulane. To obtain the hydrocarbon we used the hydroxyethyl ester mentioned. After its reduction with lithium aluminum hydride a diol was obtained in the form of a viscous oil which was oxidized with chromic anhydride.

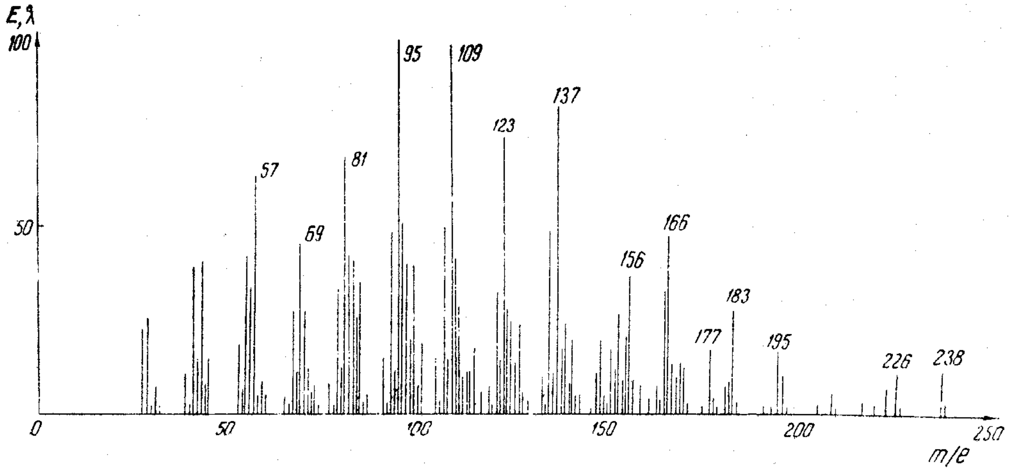
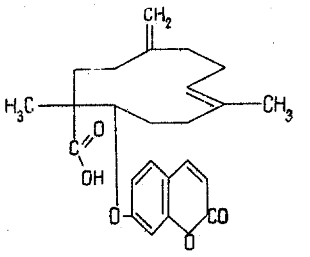
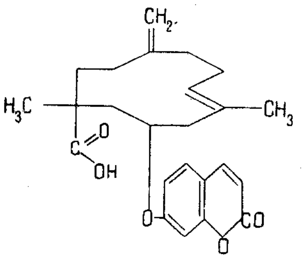


Fig. 3. Mass spectrum of the hydroxy acid $C_{15}H_{20}O_3$.

The product isolated—probably a keto aldehyde (1735 cm^{-1}—broad band)—was reduced again by Clemmensen's method and gave a hydrocarbon with the probable composition $C_{14}H_{28}$ or $C_{15}H_{30}$ the IR spectrum of which was identical with no known hydrocarbon.



I



II

Experimental

Isolation of karatavic acid. Twenty grams of the resin was dissolved in 100 ml of carbon tetrachloride, and the solution was left in the cold for 24 hr. Crystals deposited which were recrystallized three times from carbon tetrachloride; mp 89–90° C after sintering at 85–86° C; $[\alpha]_D$ − 105° (c 8; ethanol); UV spectrum: 324 mμ (log ε 3. 97); IR spectrum: 3065, 1730, 1712, 1618, 900, 840 cm^{-1}.

Found, %: C 72.58, 72.61; H 7.16, 7.14. Calculated for $C_{24}H_{28}O_5$, %: C 72.7; H 7.12.

On heating in methanol acidified with 2–3 drops of sulfuric acid, karatavic acid forms a methyl ester $C_{25}H_{30}O_5$ with mp 106–107° C; M^+, m/e 410. Under the same conditions with ethanol it forms an ethyl ester $C_{26}H_{32}O_5$ with mp 124–125° C; M^+, m/e 424.

Hydrogenation. In solution in 40 ml of glacial acetic acid, 5 g of ethyl karatavate was hydrogenated in the presence of 1 g of platinum oxide. It absorbed 1390 ml of hydrogen. A chloroform extract was washed with a sodium hydrogen carbonate solution and with water and was dried with calcium chloride, and the chloroform was distilled off. The residue was chromatographed on a column of alumina (3 × 100 cm, activity grade III). It was eluted with chloroform to yield a liquid hydroxyethyl ester, R_f 0.26 (Al_2O_3, activity grade III, solvent chloroform), n_D^{20} 1.4815; IR spectrum: 3450 (OH), 1735 cm^{-1} (CO of an ester).

Found, %: C 71.55, 71.77; H 11.10, 11.10. Calculated for $C_{17}H_{32}O_3$, %: C 71.83; H 11.27.

Saponification of the hydroxyethyl ester gave a crystalline hydroxy acid with mp 143–144° C [from a mixture of petroleum and diethyl ethers (1 : 3)], $[\alpha]_D$—20. 25° (c 3. 16; ethanol); IR spectrum: 3300, 2600, 1700 cm^{-1}.

Found, %: C 70.27, 70.27; H 10.96, 11.04. Calculated for $C_{15}H_{28}O_3$, %: C 70.35; H 10.93.

Clemmensen reduction of the keto aldehyde. A mixture of 10 parts of concentrated hydrochloric acid and 10 parts of acetic acid, followed by 1.2 g of the keto aldehyde in 40 ml of acetic acid, was added to amalgamated zinc.

The mixture was left at room temperature for 48 hr. Then it was heated in the water bath for 2 hr. A petroleum ether extract was washed with sodium hydrogen carbonate solution and with water, was dried over sodium sulfate, and the solvent was distilled off. The residue was chromatographed through a column (1 × 20 cm, Al_2O_3, activity grade II). Elution was carried out with petroleum ether. A liquid hydrocarbon was obtained with n_D^{20} 1.4780; IR spectrum: 1460, 1375, 1300, 1250, 1170, 1140, 1035, 890, 855, 740, 720 cm^{-1}.

Found, %: C 86.10; H 13.70. Calculated for $C_{15}H_{30}$ ($C_{14}H_{28}$), %: C 85.71; H 14.28.

Ozonization. At −15° C, ozone was passed through a solution of 3 g of ethyl karatavate in 20 ml of freshly distilled dry chloroform until an intense coloration was imparted to a 10% aqueous solution of potassium iodide.

The chloroform was distilled off under vacuum. The residue—a viscous yellowish oil—was heated in the boiling water bath with 100 ml of distilled water for 2 hr, 20 ml of the liquid was distilled off, and 5 ml of an aqueous solution of 2, 4-dinitrophenylhydrazine acidified with hydrochloric acid was added to it. A precipitate deposited with mp 164° C (from ethanol); this was identified as formaldehyde 2, 4-dinitrophenylhydrazone.

The microanalyses were performed by E. A. Sokolova. The IR spectra were recorded by T. V. Bukreeva on a UR-10 instrument. The NMR spectra were recorded and interpreted by V. I. Sheichenko and A. I. Kol'tsov. The mass spectra were taken by V. N. Bochkarev.

The roots of Ferula karatavica were obtained in the region of Chengel'dy, Kazakh SSR.

Conclusions

Karatavic acid has been isolated from the resin of the roots of Ferula karatavica Rgl. et Schmalh; this is an ether of umbelliferone and a hydroxy acid $C_{15}H_{24}O_3$ probably having the humulane type of hydrocarbon skeleton. Two possible structural formulas—(I) and (II)—have been proposed for karatavic acid.

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27 May 1967

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