UDC 547-314:633.88

SESQUITERPENE LACTONES FROM ARTEMISIA TAURICA

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Khimiya Prirodnykh Soedinenii, Vol. 4, No. 4, pp. 205-207, 1968

The isolation from the leaves and flower heads of Artemisia taurica Willd. (Tauric wormwood) of two sesquiterpene lactones—tauremisin and mibulactones—has been reported previously [1-3].

The presence of yet another substance, with R_f 0.90 [benzene-methanol (9 : 1) system], has been established by the thin-layer chromatography on alumina of the resin after the isolation of the lactones mentioned and also of alcoholic and chloroformic extracts from the fresh plant.

By fractional chromatography on neutral alumina, we have obtained in low yield a sesquiterpene lactone with the composition $C_{15}H_{20}O_3$, mp 118-119° C (from ethanol), $[\alpha]_D^{19}$ -120° (c5; ethanol). Its IR spectrum has absorption bands at 1780 cm^{-1} (γ-lactone) and 1711 cm^{-1} (C=O in a six-membered ring); the UV spectrum lacks maxima characterizing conjugation.

The presence of a lactone ring in the substance is also confirmed by its solubility in alkalies on heating, and the presence of a keto group by the formation of an oxime $C_{15}H_{21}O_3N$ with mp 192-194°C. By comparing the data obtained with known figures, we have come to the conclusion that the isolated lactone has not yet been reported in the literature and we have called it taurin [1].

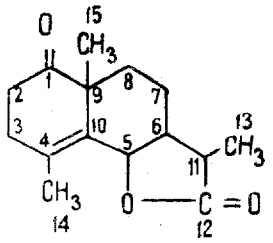
The hydrogenation of taurin in the presence of platinum oxide (according to Adams) forms a dihydro derivative $C_{15}H_{22}O_3$ with mp 169-171° C; ν_{max} 3500 cm^{-1} (OH), 1758 (γ-lactone), and 1668 cm^{-1} (C=C). The presence of an OH group in dihydrotaurin is shown by the preparation of an acetyl derivative $C_{17}H_{24}O_4$ with mp 111.5-113.5° C; ν_{max} 1770 cm^{-1} (γ-lactone), 1728, 1250 cm^{-1} (CH_3COO). Thus, the hydrogenation of taurin leads to the reduction of the keto group and the double carbon-carbon bond remains unchanged. The dehydrogenation of dihydrotaurin over selenium at 300-340° C for 30 hr gave a hydrocarbon which with picric acid formed orange needles (mp 94-95° C) giving no depression of the melting point with the picrate of 7-ethyl-1-methylnaphthalene from tauremisin. Consequently, the carbon skeleton in taurin is similar to that in tauremisin, i.e., taurin is a sesquiterpene lactone of the selinane (eudesmane) type.

In the EPR spectrum of taurin the signals of three methyl groups appear clearly—on a tertiary carbon atom (doublet 1.22 ppm), on a quaternary carbon atom (singlet 1.33 ppm), and also on a carbon atom with a double bond (singlet 1.96 ppm).

Since signals of olefinic protons are absent, two positions are possible for the double bond, i.e., C_4—C_{10} and C_6—C_{11} and a choice between these must also be made. In actual fact, the position of the signal of the methyl group on the tertiary carbon is, on the one hand, common for methyls attached to a lactone ring [4, 5] and, on the other hand, differs considerably from the position of the signals of methyl groups on a carbon atom in sp^3 hybridization to which no heteroatoms are adjacent. Consequently, it is most likely that the double bond is between carbon atoms 4 and 10. The position of the keto group was established by a comparison of the spectra of taurin [1] and dihydrotaurin.

In the spectrum of taurin there are signals with an intensity of four proton units in the 2.3-2.7 ppm region. These signals undoubtedly correspond to protons attached to carbons in the α-position with respect to a double bond and to a keto group. In dihydrotaurin, these signals are in the 2.0-2.3 ppm region, i.e., the maximum of the intensity of the signals of the protons in the α-position has shifted in the strong-field direction by approximately 0.3 ppm, which shows a comparatively marked change. Thus, it may be concluded that the keto group and the double bond are present in the same ring.

The question of the position of the keto group can be answered from a consideration of the signal of the proton on the carbon bearing the hydroxyl in dihydrotaurin. The signal is in the form of a quartet with narrow lines in the 3.52 ppm region. In view of the fact that there are no hydrogen atoms at C_9, it may be concluded that the hydroxyl is located on the neighboring atom, i.e., at C_1. This is apparently connected with the shift of the quaternary methyl to a stronger field-to 1.1 ppm. The comparatively large sum of the spin-spin interaction constants $J_{1,2a} + J_{1,2e} = 15$ Hz shows the equatorial orientation of the hydroxyl. The signal of the lactone proton (at C_5) appears in the weakest region of the field. This signal consists of a doublet (4.60 ppm, J = 10.0 Hz). The high spin-spin interaction constant shows the trans location of the protons at C_5 and C_6. The data presented above enable us to put forward the structural formula for taurin (I). It follows from this that taurin is stereoisomeric with finitin and deoxy-ψ-santonin [6].



I

Experimental

Isolation of taurin. Forty grams of the resin from the isolation of tauremisin was chromatographed on neutral alumina (activity grade IV) in a ratio of 1 : 2. A mixture of petroleum ether and benzene (9 : 1) eluted colorless crystals with mp 118–119° C (from ethanol), $[\alpha]_D^{19}$ –120° (c 5.0; ethanol).

Found, %: C 72.68, 72.71; H 8.18, 8.22; mol. wt. (Rast) 230, 234. Calculated for $C_{15}H_{20}O_3$, %: C 72.57; H 8.06; mol. wt. 248.

Taurin oxime. A mixture of 0.12 g of taurin, 0.12 g of hydroxylamine hydrochloride, 2 ml of pyridine, and 2 ml of absolute ethanol was heated at 60° C for 2 hr and then 5 ml of water was added. The crystals that deposited were recrystallized from ethanol, mp 192–194° C (decomp). Yield 0.1 g.

Found, %: C 68.83, 68.86; H 8.22, 8.20; N 5.51. Calculated for $C_{15}H_{21}O_3N$, %: C 68.44; H 8.04; N 5.32.

Dihydrotaurin. In the presence of 0.1 g of platinum oxide (Adams), 0.5 g of taurin in 60 ml of ethanol was hydrogenated until the absorption of hydrogen ceased. One mole of hydrogen was absorbed. The catalyst was filtered off and the solution was evaporated to small bulk. Colorless needles with mp 169–171° C (from ethanol) deposited.

Found, %: C 71.69, 71.71; H 8.85, 8.73. Calculated for $C_{15}H_{22}O_3$, %: C 72.01; H 8.80.

Acetyldihydrotaurin. A mixture of 0.19 g of dihydrotaurin, 2 ml of pyridine, and 4 ml of acetic anhydride was heated at 60° C for 1 hr and then water was added, and the precipitate was filtered off, washed with water, and recrystallized from ethanol; the melting point of the substance obtained was 111.5–113° C.

Found, %: C 69.90, 70.11; H 8.21, 8.29. Calculated for $C_{17}H_{24}O_4$, %: C 69.84; H 8.27.

Dehydrogenation of dihydrotaurin. A mixture of 1.8 g of dihydrotaurin and 2 g of selenium was heated at 300–340° C for 30 hr. The reaction product was extracted with petroleum ether and chromatographed on neutral alumina (activity grade I). Petroleum ether eluted 0.06 ml of a colorless liquid, a solution of which in 1 ml of absolute ethanol was mixed with a hot solution of 0.05 g of picric acid in 1 ml of absolute ethanol. Orange needles were obtained with mp 94–96° C (from ethanol), giving no depression of the melting point with 7-ethyl-1-methylnapthalene picrate (96° C) prepared similarly from tetrahydrotauremisin [2].

The UV and IR spectra were recorded by M. E. Perel'son and A. A. Kir'yanov. The microanalyses were performed by E. A. Nikonova and E. A. Plokhova.

Conclusions

The mother liquor from Artemisia taurica Willd., after the isolation of tauremisin and mibulactone, has yielded by fractional chromatography a new sesquiterpene lactone—taurin, $C_{15}H_{20}O_3$, with mp 118–119° C (from ethanol), $[\alpha]_D^{19}$ –120° (c 5.0; ethanol). The structure (I) is proposed for it.

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15 March 1967

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