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TRITERPENE GLYCOSIDES OF Hedera taurica.

II. THE STRUCTURE OF TAUROSIDES B AND C FROM LEAVES OF CRIMEAN IVY

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Two triterpene glycosides have been isolated from the leaves of Hedera taurica Carr. (Crimean ivy), family Araliaceae — taurosides B and C, for which, on the basis of the results of chemical and physicochemical methods of investigation the following structures are proposed: 3-O-α-L-arabinopyranosylhederagenin and 3-O-[O-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl]oleanolic acid.

Continuing a study of the triterpene glycosides from the leaves of Crimean ivy Hedera taurica Carr.* [1], we have isolated two weakly polar glycosides which have been called taurosides B and C, and we have established their structures.

The glycosides were isolated by the method of preparative column chromatography on silica gel followed by supplementary chromatographic purification in the form of the methyl esters at the free carboxy groups of the aglycons.

Analysis of acid hydrolysates of the glycosides with the aid of thin-layer chromatography (TLC) and paper chromatography (PC) showed that tauroside B contained hederagenin as the aglycon and tauroside C contained oleanolic acid; the carbohydrate moiety of glycoside B consisted of arabinose, and that of glycoside C of arabinose and rhamnose. The subsequent use of ^{1}H and ^{13}C NMR spectroscopy enabled the structures of the glycosides isolated to be determined completely without the use of traditional chemical methods such as methylation and periodate oxidation.

The general form of the PMR spectrum of tauroside B corresponded to the monomeric composition arabinose:hederagenin = 1:1. In a detailed analysis of the spectrum it was possible to determine the position and nature of the coupling of the majority of the skeletal protons of the monosaccharide residue (see the Experimental part). The values of the spin-spin coupling constants (SSCCs) unambiguously agreed with the α-arabino configuration of the carbohydrate moiety.

The assignment of the signals of the carbon atoms of the aglycon in the ^{13}C NMR spectrum of glycoside B (Table 1) was made by comparison with the spectrum of hederagenin taken under similar conditions [2], the downfield shift of the C-3 signal indicating the participation of the hydroxy group at this atom in the formation of a glycosidic bond. The other signals in the ^{13}C NMR spectrum belonging to the sugar residue were assigned with the aid of the method

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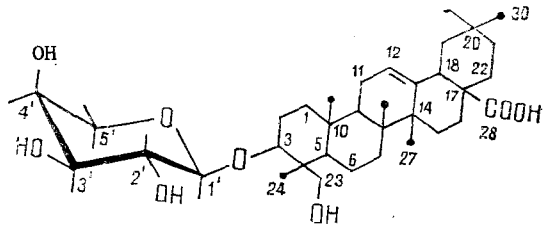
TABLE 1. Chemical Shifts of the Signals of the ^{13}C Carbon Atoms of Tauroside B (I) and Tauroside C (II) (δ, ppm, O – TMS; C_5D_5N).

Atom	Chem. shift		Atom	Chem. shift		Atom	Chem. shift	
	I	II		I	II		I	II
1	38,9	39,0	16	23,8	23,9	O–CH_3	51,8	51,8
2	26,3	26,7	17	46,2	46,2			
3	82,1	88,9	18	41,9	42,0	1′	106,8	104,9
4	43,6	39,7	19	47,1	47,1	2′	73,2	76,1
5	47,6	56,1	20	30,9	31,0	3′	74,8	73,9
6	18,3	18,7	21	34,1	34,1	4′	69,8	68,8
7	32,9	33,0	22	32,9	33,2	5′	67,1	64,8
8	39,8	39,8	23	64,5	28,3			
9	48,2	48,1	24	13,8	17,2	1″		101,9
10	37,0	37,2	25	16,2	15,7	2″		72,5
11	24,0	23,6	26	17,4	17,3	3″		72,7
12	123,0	123,0	27	26,3	26,3	4″		74,1
13	144,3	144,3	28	178,2	178,2	5″		70,0
14	42,1	42,1	29	33,3	33,3	6″		18,7
15	28,2	28,3	30	23,5	23,9			

The assignment of the signals in compound (I) between atoms 11 and 16 and atoms 17 and 19 and in compound (II) between atoms 7, 22, and 29, atoms 11, 16, and 30, and atoms 17 and 19 has been made arbitrarily. For the C-1" atom, $J_{C,H}$ = 170 Hz.

of $^{13}C_i\{^1H_i\}$ selective heteronuclear double resonance. The chemical shifts agree well with those for the C atoms in unsubstituted methyl α-L-arabinopyranoside [2]. Thus, tauroside B is 3-O-(α-L-arabinopyranosyl) hederagenin.

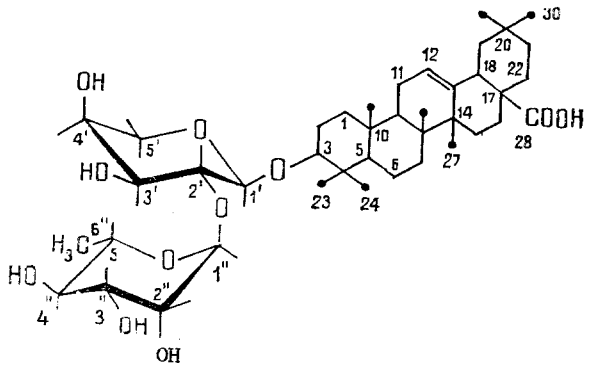


In a comparison with glycosides of established structure it can be seen that glycoside B is identical with "saponin I" from the berries of Hedera helix [3], saponin K_3 from Hedera rhombia [4], and a number of others [5].

The PMR spectrum of tauroside C corresponded to the monomeric composition rhamnose: arabinose:oleanolic acid = 1:1:1 (see the Experimental part). From the SSCCs of the series of signals of the carbohydrate residues the α-configuration of the glycosidic bond of the arabinose residue was determined unambiguously. Confirmation of the α-configuration of the glycosidic bond of the rhamnose residue (axial orientation of the substituent at C"-1) follows from the SSCC $J_{C_1",H_1"}$ = 170 Hz [6].

The chemical shifts of the signals of the ^{13}C atoms of the carbohydrate moiety of the molecule were assigned by the method of selective heteronuclear double resonance. When they were compared with the chemical shifts of the C-atoms in unsubstituted methyl α-L-rhamno- and arabinopyranosides [2], a downfield shift (4 ppm) of the C'-2 signal of the arabinose residue was observed, which can also be seen in a comparison of the chemical shifts of the C-atoms of the arabinose residues in glycosides B and C. This shows the presence of a 1 → 2 bond between the rhamnose and arabinose residues. The signals of the carbon atoms of the aglycon in the spectrum of tauroside C agree well with literature information for oleanolic acid [7], confirming the definitive structure of this glycoside.(see top of next page)

Consequently, taurosid C is 3-O-[O-α-L-rhamnopyranosyl (1 → 2)-α-L-arabinopyranosyl] oleanolic acid.



Eleutheroside K from Eleutherococcus senticosus [8], saponin P_B from Akebia quinata [9], and a saponin from Hedera nepalenis [10] have the same structure.

EXPERIMENTAL

PMR spectra were recorded on a Bruker WM-250 instrument.

We have described the isolation of tarosides B and C previously [1]. For additional purification from traces of phenolic compounds, methanolic solutions of tarosides B and C were treated with an excess of an ethereal solution of diazomethane, and the resulting methyl derivatives were rechromatographed on silica gel (L, 40-100 μm) with elution by water-saturated chloroform—methanol (9:1). After purification, the methyl derivative of tauroside B had $[\alpha]_D$ + 48° (c 2.7; pyridine), and the methyl derivative of tauroside C $[\alpha]_D$ 0° (c 3.3; pyridine).

PMR spectrum of tauroside B (250 MHz, C_5D_5N, δ, ppm, 0 — TMS): 4.93, d, $J_{1',2'}$ = 7.5 Hz (H-1'); 4.37, dd, $J_{2',3'}$ = 9.0 Hz (H-2'); 4.03, dd, $J_{3',4'}$ = 3.2 Hz (H-3'); 4.23, dd, $J_{5e,4'}$ = 3.2 Hz, $J_{5a,5e}$ = 10.5 Hz (H-5e'); 4.1—4.3 m (H-4', H-5'e), H-23A); 3.6—3.75 m (H-5'a,O-CH_3, H-23B); 3.03, dd, $J_{3,2e}$ = 3.8 Hz, $J_{3,2a}$ = 14.0 Hz (H—3); 5.34, br.t (H-12); 1.13, s, 0.93, s, 0.89, s, 0.88, s, 0.86, s, 0.80, s (6-CH_3).

PMR spectrum of tauroside C (250 MHz, C_5D_5N, δ, ppm, 0 — TMS): 4.85, d, $J_{1',2'}$ = 6.0 Hz (H-1'); 4.50, t, $J_{2',3'}$ = 6.0 Hz (H-2'); 6.06, d, $J_{1'',2''}$ = 1.8 Hz (H-1''); 4.69, dd, $J_{2'',3''}$ = 3.5 Hz (H-2''); 4.57, dd, $J_{3'',4''}$ = 9.5 Hz (H-3''); 4.25, t, $J_{4'',5''}$ = 9.5 Hz (H-4''); 4.53, dd, $J_{5'',6''}$ = 6.0 Hz (H-5''); 1.58, d (6''-CH_3); 4.1—4.4, m (H-3', H-4', H-5'e); 3.6—3.9 m (H-5'a, O—CH_3); 3.20, dd, $J_{3,2e}$ = 4.5 Hz, $J_{3,2a}$ = 12 Hz (H-3); 5.34, br.t (H-12); 1.20, s, 1.14, s, 1.03, s, 0.90, s, 0.89, s, 0.83, s, 0.80, s, (7-CH_3).

A solution of 2 mg of tauroside B or C in 0.2 ml of dioxane was treated with 0.2 ml of 2 N aqueous sulfuric acid and hydrolysis was carried out at 100°C for 2 h. After extraction of the aglycons with chloroform, hederagenin and oleanolic acid were identified in glycosides B and C, respectively by TLC comparison with authentic samples.

To determine their monosaccharide compositions, 2 mg of glycosides B and C in 0.2 ml of diozane were each treated with 0.2 ml of 2 N aqueous trifluoroacetic acid, and the mixtures were heated to 100°C for 2 h. In the hydrolysates, using PC (solvent system butanol—acetic acid—water (4:1:5)), arabinose was identified in the case of glycoside B, and arabinose and rhamnose in the case of glycoside C.

SUMMARY

The structures of two weakly polar triterpene glycosides from the leaves of Crimean ivy have been identified by ^1H and ^{13}C NMR spectroscopy. Tauroside B is 3-O-α-L-arabinopyranosyl-hederagenin, and tauroside C 3-O-[O-α-L-rhamnopyranosyl-(1 → 2)-α-L-arabinopyranosyl] oleanolic acid.

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SYNTHESIS OF CONVALLOSIDE

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The known natural diglycoside convalloside — strophanthidin 3β-O-[4-O-β-d-glucopyranosyl-α-L-rhamnopyranoside] — has been synthesized. The synthesis was carried out by the Koenigs-Knorr method via the preparation as intermediates of convallatoxin and its 2,3-isopropylidene derivative. Selectivity of glycosylation was achieved by the preliminary protection of the two OH groups in the cardenolide L-rhamnoside (convallatoxin).

More than 20 cardiac monoglycosides obtained by the glycosylation of cardenolides and bufadienolides by the Koenigs—Knorr method, and also by the orthoester method, are known. The possibilities of the synthesis of glycosides with chain-like carbohydrate units attached as in nature to C-3 of the aglycons has been investigated to a smaller degree. On this level, two synthesized diglycosides are known: K-strophanthin-β [1-3] and erythroside [4]. The synthesis of the first starts with cymarin, which has only one reactive OH group and therefore does not differ basically from the synthesis of monoglycosides. Erythroside is synthesized [4] by using an erysimin monoglycoside having two reactive OH groups in the carbohydrate unit. Definite selectivity of glycosylation at C-4" is achieved because of the conformational differences of the OH group in the D-digitoxose unit.

It appears to us that the use of L-rhamnosides in such reactions is also possible, but with the preliminary protection of two OH groups. In cardenolide L-rhamnosides, which are fairly common monosides, the OH groups at C-2' and C-3' occupy the cis position, which enables them to be protected by the formation of isopropylidene derivatives. We have performed the synthesis of the known natural diglycoside convalloside (III) via the isopropylidene derivative of convallatoxin (II). The convallatoxin necessary for this purpose was synthesized from the aglycon strophanthadin (I) and 2,3,4-tri-O-acetyl-1-bromo-L-rhamnose. The acetonide (II) was obtained by the condensation of convallatoxin with acetone in the presence of copper sulfate.

At both stages, glycosylation was carried out by the Koenigs-Knorr method in boiling dichloroethane [5] with the use of a mixture of silver carbonate and mercury oxide as HBr acceptor. The protective acetyl and isopropylidene groups were removed by controlled alkaline and acid hydrolysis, respectively.

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