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STRUCTURE OF THE PRODUCTS OF ACID HYDROLYSIS OF PANAXOSIDE A

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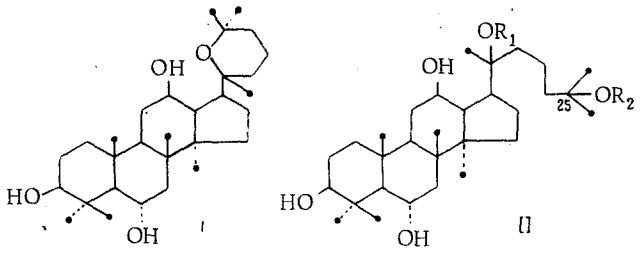
We have previously shown [1] that the acid hydrolysis of panaxoside A—a triterpene glycoside of the dammarane series from Panax ginseng C. A. Meyer—forms an equilibrium mixture of substances A_1–A_6 representing the products of a change in the native genin under the conditions of hydrolysis. It was found that panaxosides B and C give the same mixture of substances on hydrolysis. For one of them—panaxatriol (A_6)—we [2] and Shibata [3] established structure I. In the present paper we give information on the structure of other components of the mixture (A_1, A_2, and A_5, which partially confirm the structure that we proposed previously for the native genin of panaxoside A [1]. The isolation of substances A_1, A_2, and A_5, the empirical formulas and analytical data of which are given in Table 1, was carried out by chromatography on alumina and silica gel [1].



Substances A_1, A_2, and A_5 and their acetates were studied by NMR spectroscopy. The investigation of the methyl region of the NMR spectra permitted deductions concerning the position of hydroxy and methoxy groups in the side chain. The chemical shifts of the signals of the methyl groups are given in Table 2. The signals of the methyl groups of rings A, B, C, and D and the signals of the protons at C_3, C_6, and C_{12} have similar chemical shifts for all these substances, which confirms the identity of their skeletal structure.

The shift of the signals of the three methyl groups of the side chain into the weak field (1.10 ppm—1 CH_3 and 1.15 ppm—2 CH_3) as compared with the signals of the methyl groups of the isooctane side chain [4] in the spectra of A_5 and A_5 acetate shows that the methyl groups are adjacent to oxygen-containing functions, and the absence of splitting of the signals shows that the oxygen functions are tertiary. In view of the presence in A_5 of two methoxy groups and the identity of its skeleton with that of panaxatriol, the signal at 1.10 ppm must be assigned to the 21-methyl group (OCH_3 at C_{20}) and the signal at 1.15 ppm to the 26- and 27-methyl groups (OCH_3 at C_{25}). In the spectrum of the acetate* of the very polar substance A_1 containing five hydroxy groups, the signal at 1.12 ppm corresponds to the 21-methyl group (OH at C_{20}) [5] and that at 1.22 ppm to the 26- and 27-methyl groups (OH at C_{25}).

On comparing the spectra of the acetates of A_2 and the acetates of the preceding substances and taking the analytical data (4 OH and 1 OCH_3) into account, it can be seen that an OH group is located at C_{20} (1.12 ppm), and the OCH_3 group at C_{25} (1.16 ppm). The absence of a signal at 1.22 ppm excludes the location of a hydroxy group at C_{25}.

Thus, it has been established by NMR spectroscopy that the hydroxy and methoxy groups of the side chains of substances A_1, A_2, and A_5 are tertiary and are located at C_{20} and C_{25}. In this case, substance A_5 must be ascribed the structure of 20,25-di-O-methyldammarane-3β, 6α,12β,20ξ,25-pentaol (II, $R_1 = R_2 = CH_3$), substance A_2 the structure of 25-O-methyldammarane-3β, 6α, 12β, 20ξ, 25-pentaol (II, $R_1 = H$; $R_2 = CH_3$); and substance A_1 the structure of dammarane-3β, 6α, 12β, 20ξ, 25-pentaol (II, $R_1 = R_2 = H$). This is confirmed by the results of mass spectroscopy [6] and agrees with the data for the side chain of the products of the acid hydrolysis of panaxoside F [7].

Starting from the experimental fact of the production of a full acetate of panaxoside A [8]—mp 242–246° C, $[\alpha]_D^{20} \pm 3°$ (c 3.7; chloroform)—and, consequently, the absence of tertiary hydroxy groups from panaxoside A, we came to the conclusion that the tertiary hydroxy groups in substances A_1–A_5 have arisen as a consequence of the hydration (addition of CH_3OH) of two unsaturated bonds of the native genin under the hydrolysis conditions. An analogous example of the hydration of a multiple bond has been described for methyl leucotylate [9], the acid treatment of which (5% HCl, C_2H_5OH, boiling for 6 hr) led to the production of methyl isoleucotylate, the conversion taking place by a dehydration-hydration reaction.

*The spectrum of A_1 in $CDCl_3$ was not obtained because of its low solubility.

Table 1

Substance	Mp, °C	$[\alpha]_D^{22}$, deg.	Found, %				Empirical formula	Calculated, %			
			C	H	H_{act}	OCH_3		C	H	H_{act}	OCH_3
A_1	252–254	+30 [c 1.8; CH_3OH—$CHCl_3$ (5:1)]	71.27 71.05	10.96 10.75	—	0.00 —	$C_{30}H_{54}O_5 \cdot 1/2\ H_2O$	71.52	11.00	—	—
A_2	253–254	+30.5 (c 3.14; $CHCl_3$)	71.51 71.62	11.34 11.40	—	4.82 5.40	$C_{30}H_{53}O_4(OCH_3) \cdot 1/2\ H_2O$	71.90	11.11	—	5.98
A_5	159–163	+34 (c 1.94; $CHCl_3$)	73.66 73.40	11.15 10.97	0.63 0.213	10.15 10.20	$C_{30}H_{19}(OH)_3(OCH_3)_2$	73.51	11.18	0.58	11.8
Acetate of A_2	162.5–163.5	+15.5 (c 2.06; $CHCl_3$)	70.48 70.72	9.73 9.50		4.70 4.75	$C_{37}H_{62}O_8$	69.99	9.84	0.34	5.22

Table 2

Compound	4α	4β	10β	8β	14α	20	25	25	OMe	12βOH	3βOH 5αOH	3αH* triplet	12αH* quartet	6βH* quartet
Panaxatriol	0.89	0.95	1.15	1.03	0.89	1.18	1.22	1.28	—	6.25	1.94	3.15	3.55	4.08
Diacetate of panaxatriol	0.93	1.05	1.05	1.14	0.93	1.20	1.24	1.28	—	6.25	—	4.47	3.55	5.37
20,25-Di-O-methyladamaranepentaol (A_5)	0.90	0.86	1.15	1.04	0.90	1.10	1.15	1.15	3.18	5.77	1.95	3	3.5	4.05
Diacetate of 20, 25-di-O-methyldammarane-pentaol (diacetate of A_5)	0.94	1.06	1.06	1.13	0.94	1.13	1.16	1.16	3.19	—	—	4.30	3.55	5.40
Triacetate of 25-O-methyldammaranepentaol (triacetate of A_2)	0.93	1.00	1.00	1.15	1.00	1.12	1.16	1.16	3.18	—	—	4.55	4.85	5.40
Triacetate of dammaranepentaol (triacetate of A_1)	0.93	1.02	1.02	1.15	0.93	1.12	1.22	1.22	—	—	—	4.40	4.40	5.35

*The spin-spin coupling constant τ (5-10 Hz) shows the axial position of the hydrogen atoms, i.e., equatorial arrangement of the hydroxyls.

On the basis of the data given, the position of one multiple bond of the native genin must be assigned to the side chain. The second multiple bond may be located in ring D or occupy an exocyclic position ($\Delta^{17(20)}$). The position of the multiple bonds on the native genin of panaxoside A is being studied.

Conclusions

The substances obtained in the acid hydrolysis of panaxosides A, B, and C have been isolated and characterized. The structures of these substances have been established from a combination of chemical data and the results of NMR spectroscopy.

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