TRITERPENE GLYCOSIDES OF *Astragalus* AND THEIR GENINS.

V. STRUCTURE OF CYCLOSIEVERSIOSIDE F

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A new glycoside of the cycloartane series has been isolated from the roots of the plant *Astragalus sieversianus* Pall. and it has been shown to be cyclosieversigenin 6-O-β-D-glucopyranoside 3-O-β-D-xylopyranoside.

We have previously described the isolation from the roots of *Astragalus sieversianus* Pall. of eight glycosides and have established the structure of one of them — cyclosieversioside E [1]. In the present paper we consider the determination of the structure of substance F, which we have called cyclosieversioside F (I).

It was found by the GLC method [2] that glycoside (I) contains one residue each of D-xylose and D-glucose. The PMR spectrum of cyclosieversioside F, just like that of cyclosieversioside E [1], contains in the strong-field region at 0.46 ppm a one-proton doublet (J = 3.8 Hz) belonging to one of the protons of a cyclopropane ring. On this basis, we assign glycoside (I) to the compounds of the cycloartane series. This hypothesis was confirmed by the identification of cyclosieversigenin (II) [3] as the genin in the products of the Smith degradation of the compound under investigation [4].

The Hakomori methylation [5] of cyclosieversioside F led to the formation of the permethylate (III). The products of the acid hydrolysis of this substance were found to contain 2,3,4,6-tetra-O-methylglucopyranose, 2,3,4-tri-O-methylxylopyranose, and the 16,25-dimethyl ether (IV). In its physicochemical constants and special characteristics, compound (IV) proved to be identical with the 16,25-dimethyl ether of sieversigenin obtained previously in the acid cleavage of the permethylate of cyclosieversioside E [1].

In the ^{13}C NMR spectrum of cyclosieversigenin (II), the signals from the C-3, C-6, and C-16 carbon atoms, which bear secondary hydroxy groups, are present at, respectively, 78.2, 68.3, and 73.4 ppm. In the spectrum of cyclosieversioside F, the signals of the corresponding carbon atoms are located at 88.5, 79.2, and 73.4 ppm. Consequently, a glycosylation effect is undergone only by the atoms C-2 (+10.3 ppm) and C-6 (+10.9 ppm) [6], while the chemical shift of the C-16 signals remains unchanged.

According to all the facts given, cyclosieversioside F is a bisdesmosidic glycoside in which the sugar residues are attached to the hydroxy groups at C-3 and C-6.

The acid hydrolysis of bioside (I) with dilute sulfuric acid led to the monosides (V) and (VI). It was established by GLC that the progenin (V) contained a D-xylose residue, and the monoside (VI) contained a D-glucose residue. The positions of attachment of the sugars were ascertained by a comparative analysis of the characteristics of the ^{13}C NMR spectra of cyclosieversigenin (II) and the monosides (V) and (VI). In the spectrum of the progenin (V), the values of the chemical shifts of the C-3 and C-6 carbon atoms are, respectively, 88.7 and 68.1 ppm, while in the case of the progenin (VI), the signals from these atoms are located at 78.3 and 79.7 ppm. A comparison of these facts with those for cyclosieversigenin (II) (78.2 and 68.3) unambiguously shows that in the progenin (V) the C-3 atom undergoes a glycosylation effect, and in the progenin (VI) it is the C-6 atom. It follows from this that in the monoside (V) the xylose residue is attached through the hydroxyl at C-3, and in the monoside (VI) the glucose residue is attached through the hydroxyl at C-6.

The results of a calculation of molecular rotation differences [7] showed that the D-xylose and D-glucose are attached to the aglycone by β-glycosidic bonds.

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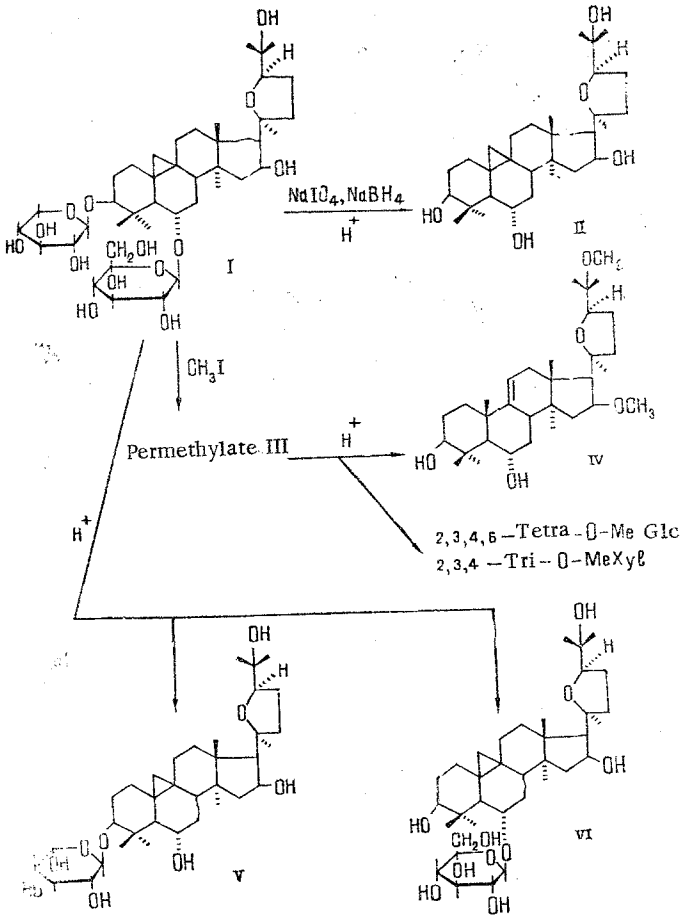

Thus, cyclosieversioside F is cyclosieversigenin 6-O-β-D-glucopyranoside 3-O-β-D-xylopyranoside.

EXPERIMENTAL

For general observations and methods of isolation, see [1] and [3]. PMR spectra were taken in C_5D_5N on a JNM-4H-100/100 MHz instrument (δ, O-HMDS), and ^{13}C NMR spectra on a Varian CFT-20 instrument in C_5D_5N (δ, O-TMS).

Cyclosieversioside F (substance F) (I). $C_{41}H_{68}O_{14}$, mp 247-249°C (from methanol), $[\alpha]_D^{23}$ +36.6 ± 2° (c 0.47; methanol); ν_{max}^{KBr}, cm^{-1}: 3300-3500 (OH), 3042 (CH_2 of a cyclopropane ring). PMR spectrum (δ, ppm): 0.46 (H at C-19, d, J = 3.8 Hz); 0.81 (CH_3, s); 1.16 (CH_3 × 3, s); 1.26 (CH_3, s); 1.42 (CH_3, s); 1.82 (CH_3, s). By the GLC method [2], D-xylose and D-glycose residues in a ratio of 0.99 1.00 were found in cyclosieversioside F.

Cyclosieversigenin (II) from (I). A solution of 500 mg of cyclosieversioside F (I) in 100 ml of aqueous methanol (1:1) was treated with 2.1 g of sodium periodate, and the mixture was stirred for 2 h. The oxidant that had not reacted was decomposed with ethylene glycol. The methanol was evaporated off, and the residue was treated with 50 ml of water and was extracted with chloroform. The chloroform was distilled off and the new residue was treated with 30 ml of methanol and 1.5 g of sodium tetrahydroborate. The reaction mixture was heated at 80°C for 7 h, after which it was acidified to 2.0 and was left at room temperature for 15 h. The hydrolysis products were extracted with chloroform. The solvent was evaporated off, and the residue was chromatographed on a column of silica gel. On elution with ethyl acetate, 180 mg of cyclosieversigenin (II) was isolated, with mp 239-243°C (from methanol), $[\alpha]_D^{20}$ +15.0 ± 2° (c 1.60; methanol) [3].

Permethylate of Cyclosieversioside F (III) from (I). In small portions, 2.0 g of sodium hydride was added to a solution of 2 g of cyclosieversioside F (I) in 300 ml of dry dimethyl sulfoxide. After 30 min, 25 ml of methyl iodide was added dropwise and the reaction mixture was then left for 5 h. All the operations were carried out at room temperature with stirring.

The reaction products were poured into 400 ml of an aqueous solution of sodium hyposulfite and exhaustively extracted with chloroform. The residue obtained after the evaporation of the combined extracts was chromatographed on a column of silica gel with elution first by benzene and then with benzene–ethyl acetate (1:1). This led to the isolation of 700 mg of the crystalline permethylate (III), $C_{50}H_{86}O_{14}$, mp 184-186°C (from ethanol), $[\alpha]_D^{20}$ +53.4 ± 2° (c 1.11; chloroform). ν_{max}^{Nujol}, cm^{-1}: 3055 (>CH_2 of a cyclopropane ring). There was no absorption in the region of hydroxy groups. PMR spectrum (δ, ppm): 0.47 (H at C-19, broadened singlet); 0.94 (CH_3, s); 1.11 (CH_3 × 2, s); 1.18 (CH_3, s); 1.31 (CH_3, s); 1.33 (CH_3, s); 1.48 (CH_3, s); 3.05-3.60 (OCH_3 × 9, s); 4.51 (2 H, anomeric protons, d, J = 7.5 Hz). M^+ 910.

Acid Hydrolysis of the Permethylate (III). A solution of 700 mg of the permethylate (III) in 100 ml of methanol was treated with 100 ml of 15% methanolic sulfuric acid, and the reaction mixture was heated in the boiling water bath for 7 h. After cooling, 200 ml of water was added, the methanol was distilled off, and the precipitate that had deposited was separated off and was chromatographed on a column of silica gel with elution by the benzene–acetone (3:1) system. In this way, 35 mg of compound (IV) was isolated: $C_{32}H_{54}O_5$, mp 220-222°C (from methanol), $[\alpha]_D^{20}$ +122.3 ± 2° (c 0.61; chloroform), identical with an authentic sample of the 16,25-dimethyl ether of sieversigenin [1].

The aqueous solution was boiled for 7 h. After cooling, it was neutralized with barium carbonate, the precipitate was separated off, and the filtrate was evaporated. The residue was found by TLC in the benzene–acetone (2:1) system, and also by the GLC method [8], to contain 2,3,4,6-tetra-O-methyl-D-glucopyranose and 2,3,4-tri-O-methyl-D-xylopyranose.

Partial Hydrolysis of Cyclosieversioside F (I) to the Monosides (V) and (VI). A solution of 2.0 g of cyclosieversioside F in 200 ml of methanol was treated with 200 ml of a 0.5% aqueous solution of sulfuric acid and the mixture was heated in the boiling water bath for 4 h. After cooling, the reaction products were extracted with chloroform, the solvent was distilled off, and the residue was separated on a column of silica gel. Elution with chloroform–methanol (9:1) gave 80 mg of cyclosieversigenin (II) with mp 239-242°C. Washing the column with the chloroform–methanol (7:1) system led to the isolation of 150 mg of cyclosieversigenin 3-O-β-D-xylopyranoside (V), $C_{35}H_{58}O_9$, mp 259-261°C (from methanol), $[\alpha]_D^{20}$ +42.0 ± 2° (c 0.62; methanol). PMR spectrum (δ, ppm): 0.44 (H at C-19, broadened singlet); 0.87 (CH_3, s); 1.19 (CH_3 × 3, s); 1.29 (CH_3, s); 1.44 (CH_3, s); 1.83 (CH_3, s). It was shown by the GLC method [2] that the progenin (V) contained a D-xylose residue.

When the elution of the column was continued with the same mixture of solvents, 700 mg of cyclosieversigenin 6-O-β-glucopyranoside (VI) was obtained; $C_{36}H_{60}O_{10}$, mp 242-244°C (from methanol), $[\alpha]_D^{20}$ +36.0 ± 2° (c 1.42 methanol). PMR spectrum (δ, ppm): 0.51 (H at C-19, broadened singlet); 0.79 (CH_3, s); 1.15 (CH_3 × 3, s); 1.24 (CH_3, s); 1.43 (CH_3, s); 1.78 (CH_3, s). According to the results of GLC, the progenin (VI) contained a D-glucose residue.

CONCLUSION

From the roots of the plant *Astragalus sieversianus* Pall. a new glucoside of the cycloartane series has been isolated and it has been shown to be cyclosieversigenin 6-O-β-D-glucopyranoside 3-O-β-D-xylopyranoside.

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