TRITERPENE GLYCOSIDES OF *Astragalus* AND THEIR GENINS.

IX. ASKENDOSIDE D FROM *Astragalus taschkendicus*

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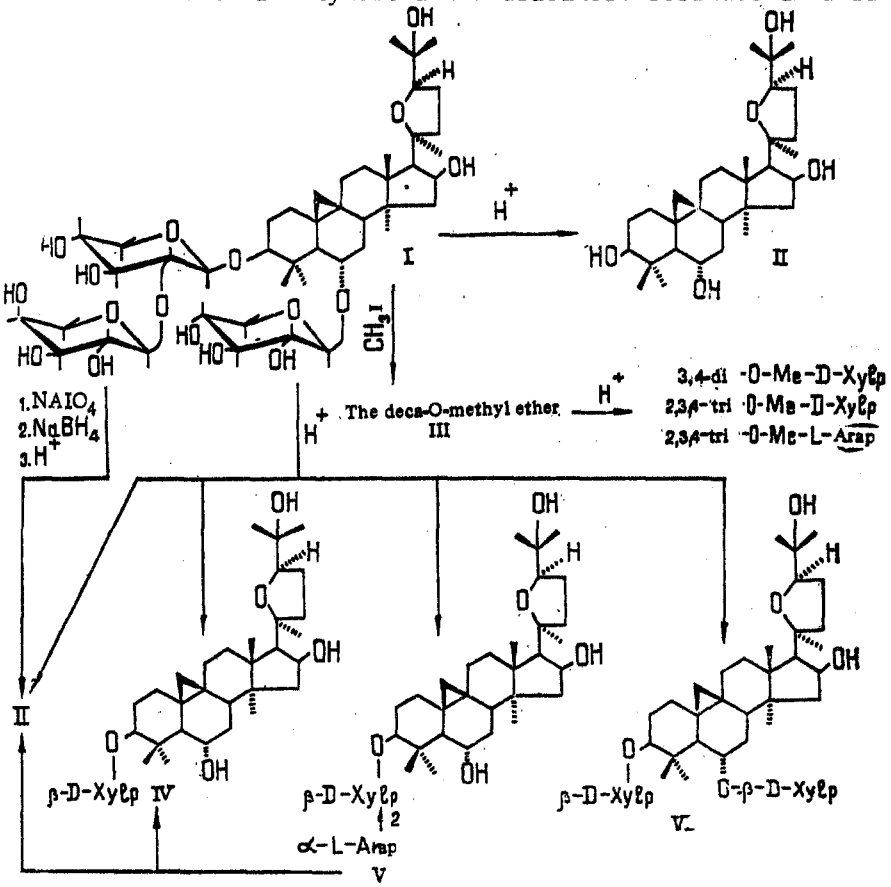
A new glycoside of the cycloartane series — askendoside D — has been isolated from the roots of the plants *Astragalus taschkendicus* Bge., and on the basis of chemical transformations and spectral characteristics its structure has been established as 20S,24R-epoxycycloartane-3β,6α,16β,25-tetraol 3-O-[O-α-L-arabinopyranosyl-(1 → 2)-β-D-xylopyranoside] 6-O-β-D-xylopyranoside.

Continuing study of the isoprenoids isolated from the plant *Astragalus taschkendicus* Bge. (family Leguminosae) [1, 2], we have now established the structure of substance F [1] and have named it askendoside D (I).

The presence of 1-proton doublet at 0.50 ppm in the PMR spectrum of compound (I) and also of an absorption band at 3040 cm^{-1} in the IR spectrum [3] permitted the new glucoside to be assigned to derivatives of the cycloartane series [4]. This conclusion was confirmed both by acid hydrolysis and by Smith degradation [5] of the glycoside (I). Both reactions led to a genin which was identified as cyclosiversigenin (II) [2, 6].

It was shown with the aid of GLC [7, 8] and TLC that the carbohydrate moiety of the askendoside D molecule consists of D-xylose and L-arabinose residues in a ratio of 2:1.



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To elucidate the structure of the carbohydrate chain, askendoside D was subjected to Hakomori methylation [9]. From the products of the methylation reaction we isolated the deca-O-methyl ether (III) (M^+ 1026). By GLC [10] and TLC in the presence of authentic samples [11, 12], we established that the carbohydrate moiety of the methyl ether (III) contained 2,3,4-tri-O-methyl-D-xylopyranose, 3,4-di-O-methyl-D-xylopyranose, and 2,3,4-tri-O-methyl-L-arabinopyranose residues. As can be seen from the set of methylated monosaccharides, glycoside (I) has one molecule of D-xylose and one molecule of L-arabinose as terminal carbohydrates. There is no branching in the sugar chain. Consequently, askendoside D is a bisdesmosidic glycoside.

Glycoside (I) was subjected to partial hydrolysis. From the hydrolysis products of glycoside (I), in addition to cyclosiversigenin (II), we isolated the progenins (IV), (V), and (VI).

It was shown by the GLC method that progenin (IV) contained one D-xylose residue; progenin (V), D-xylose and L-arabinose residues in a ratio of 1:1; and progenin (VI), two D-xylose residues.

From its physicochemical constants, spectral characteristics, and a TLC comparison with authentic samples, the monoside (IV) was identified as cyclosiversigenin 3-O-β-D-xylopyranoside [13] and bioside (VI) as cyclosiversioside E [12].

The formation of cyclosiversioside E from the bisdemoside (I) unambiguously showed that in askendoside D the carbohydrate units were attached to the cyclosiversigenin through the hydroxy groups at C-3 and C-6.

In order to elucidate the structure of the progenin (V), we carried out the partial hydrolysis of this glycoside, which led to the monoside (IV). This fact, in combination with the presence of 3,4-di-O-methyl-D-xylopyranose in a hydrolysate of the deca-O-methyl ether (III) showed that in the bioside (V) the L-arabinose residue was attached to the hydroxy group at C-2 of a D-xylose residue. A molecular rotation difference calculation showed the α configuration of the glycosidic center of the L-arabinose residue [14]. Consequently, there was no doubt that progenin (V) was cyclosiversigenin 3-O-[O-α-L-arabinopyranosyl-(1 → 2)-β-D-xylopyranoside].

In the PMR spectrum of the methyl ether (III) ($CDCl_3$) the anomeric protons of the two D-xylopyranose residues resonated at 4.26 and 4.34 ppm and that of the L-arabinopyranose residue at 4.54 ppm, in the form of doublets with spin–spin coupling constants of 7 Hz.

The facts given show that the pyranose rings of the monosaccharides have the C1 conformation and, consequently, the anomeric centers of the D-xylose residues have the β configuration and that of the L-arabinose residue the α configuration [15, 16].

Thus, askendoside D has the structure of cyclosiversigenin 3-O-[O-α-L-arabinopyranosyl)-(1 → 2)-β-D-xylopyranoside] 6-O-β-D-xylopyranoside.

EXPERIMENTAL

For general observations see [1, 11]. The following solvent systems were used: 1) chloroform–methanol (15:1); 2) ethyl acetate; 3) butanol–methanol–water (5:3:1); 4) benzene–ethyl acetate (1:1); 5) chloroform–methanol–water (70:23:4); 6) chloroform–methanol (10:1).

PMR spectra were taken in $CDCl_3$ or C_5D_5N on a Varian XL-100-15 instrument (δ, ppm, O – HMDS).

For the isolation of the isoprenoids of *Astragalus taschkendicus* Bge. see [1, 2].

Askendoside D (I). Substance F [1], $C_{45}H_{74}O_{17}$, mp 235-236°C (from aqueous methanol), $[\alpha]_D^{20} -9.1 \pm 2°$ (*c* 1.1 ; pyridine). ν_{max}^{KBr}, cm^{-1}: 3512, 3450-3285 (OH), 3035 (CH_2 of a cyclopropane ring). PMR (C_5D_5N), ppm: 0.50 (1 H at C-19, d, ^2J = 4 Hz); 1.04 (3 H, s, CH_3); 1.16 (6 H, s, 2 CH_3); 1.20 (3 H, s, CH_3); 1.26 (3 H, s, CH_3); 1.44 (3 H, s, CH_3); 1.66 (3 H, s, CH_3); 4.72 (2 H, d, $^3J \approx 6$ Hz, 2 anomeric protons of D-xylopyranose residues); 5.04 (1 H, d, ^3J = 7 Hz; anomeric proton of a L-arabinopyranose residue).

Cyclosiversigenin (II) from Askendoside D (I). A solution of 200 mg of askendoside D in 100 ml of methanol containing 0.5% of sulfuric acid was boiled on the water bath for 1.5 h. Then the reaction mixture was diluted with water to 300 ml and the methanol was distilled off. The precipitate that deposited was filtered off, washed with water, dried,

and chromatographed on a column with elution by system 1. This gave 70 mg of the genin (II) with mp 239-241°C (from methanol); $[\alpha]_D^{30}$ +52±2° (*c* 1,2; methanol). The genin (II) was identical with an authentic sample of cyclosiversigenin [2, 6], as was shown by R_f values in TLC (systems 1 and 2) and the indices of the IR, mass, and PMR spectra.

The aqueous solution was evaporated to a volume of 50 ml and was boiled on the water bath for 5 h. After neutralization with ARA-8p anion-exchange resin, D-xylose and L-arabinose were detected in the filtrate by TLC (system 3) in comparison with authentic samples. GLC showed the presence of the sugars in the askendoside D molecule in a ratio of 1.00:0.45.

The Deca-O-Methyl Ether of Askendoside D (III) from (I). With constant stirring, 0.5 g of sodium hydride was added in small portions to 0.507 g of askendoside D in 50 ml of dry dimethyl sulfoxide. Then 6 ml of methyl iodide was added dropwise to the reaction mixture and it was shaken at room temperature for 4 h, after which it was poured into 200 ml of a 2% solution of sodium hyposulfite and was exhaustively extracted with chloroform. The chloroform extract was washed with water, dried over anhydrous sodium sulfate, and evaporated. The methylation procedure was repeated three times. The reaction products were separated by column chromatography with elution by system 4. This gave fractions containing 118 mg of the deca-O-methyl ether (III), $C_{55}H_{94}O_{17}$, $[\alpha]_D^{28}$ 0 ±3° (*c* 0.56; chloroform). The IR spectrum lacked absorption due to hydroxy groups. M^+ 1026. PMR ($CDCl_3$), ppm: 0.10 (1 H at C-19, d); 0.42 (1 H at C-19, d); 0.89 (3 H, s, CH_3); 0.92 (3 H, s, CH_3); 1.03 (3 H, s, CH_3); 1.11 (3 H, s, CH_3); 1.15 (6 H, s, 2 CH_3); 1.20 (3 H, s, CH_3); 3.07 (3 H, s, OCH_3); 3.20 (3 H, s, OCH_3); 3.32 (3 H, s, OCH_3); 3.39 (3 H, s, OCH_3); 3.41 (6 H, s, 2 OCH_3); 3.46 (3 H, s, OCH_3); 3.52 (3 H, s, OCH_3); 3.54 (6 H, s, 2 OCH_3); 4.26 (1 H, d, ^3J = 7 Hz, anomeric proton of D-xylopyranose); 4.34 (1 H, d ^3J = 7 Hz, anomeric proton of D-xylopyranose); 4.55 (1 H, d, ^3J = 7 Hz, anomeric proton of L-arabinopyranose).

Hydrolysis of the Deca-O-methyl Ether (III). A solution of 80 mg of the deca-O-methyl ether of askendoside D (III) in 25 ml of methanol containing 0.5% of sulfuric acid was boiled for 1.5 h. The reaction mixture was poured into 50 ml of water and the methanol was evaporated off. The resulting precipitate was filtered off. It proved to be a mixture of difficultly separable products. The aqueous solution was evaporated to a volume of 20 ml and was boiled on the water bath for another 5 h. After cooling, the reaction mixture was neutralized with ARA-8p anion-exchange resin, which was then filtered off. After the solvent had been distilled off, 3,4-di-O-methyl-D-xylopyranose, 2,3,4-tri-O-methyl-D-xylopyranose, and 2,3,4-tri-O-methyl-L-arabinopyranose were detected in the residue with the aid of GLC [10] and TLC in the presence of authentic samples [11, 12].

Partial Hydrolysis of Askendoside D (I). A solution of 2.5 g of askendoside D in 500 ml of methanol containing 0.5% of sulfuric acid was boiled on the water bath for 40 min. The reaction mixture was diluted with 500 ml of water, and part of the methanol was evaporated off. The solution was diluted with water to a volume of 1 liter. The reaction products were extracted with butanol (4 × 200 ml). The butanolic extract was washed with water to neutrality. The dry residue obtained after the evaporation of the solvents (1.94 g) was chromatographed on a column with elution by systems 1 and 5 in succession. The fractions collected on elution by system 1 yielded 500 mg of cyclosiversigenin (II) with mp 239-241°C (from methanol), $[\alpha]_D^{29}$ +56.6±2° (*c* 1.59; methanol), which was shown to be identical with an authentic sample according to IR, mass, and PMR spectra and to mobilities in TLC (systems 1 and 2).

Subsequent elution of the column with system 5 and rechromatography of the intermediate fractions obtained in the same system led to the isolation of the individual glycosides (IV), (V), and (VI).

Cyclosiversigenin 3-O-β-D-xylopyranoside (IV) from (I). After recrystallization from methanol, progenin (IV) (407 mg) had the composition $C_{35}H_{58}O_9$, mp 263-264°C $[\alpha]_D^{21}$ +40±2° (*c* 0,5; methanol). According to GLC, glycoside (IV) contained one D-xylose residue. The agreement of the indices of the PMR and IR spectra of the monoside (IV) with those for cyclosiversigenin 3-O-β-D-xylopyranoside [13], and also the similar chromatographic behaviors on TLC (in systems 5 and 6) of these compounds showed their identity.

Cyclosiversigenin 3-O-[O-α-L-arabinopyranosyl-(1 → 2)-β-D-xylopyranoside] (V) from (I). Progenin (V) (153 mg), $C_{40}H_{66}O_{13}$, had mp 206-208°C (from ethyl acetate), $[\alpha]_D^{21}$ + 26.4 ± 2° (*c* 1.06; methanol). ν_{max}^{KBr}, cm^{-1}: 3500-3340 (OH), 3050 (CH_2 of a cyclopropane ring). GLC showed the presence in the glycoside (V) molecule of D-xylose and L-arabinose residues in a ratio of 1:1.33. PMR (C_5D_5N), ppm: 0.21 (1 H at C-19, d, ^2J = 4 Hz); 0.52 (1 H at C-19, d, ^2J = 4 Hz); 0.91 (3 H, s, CH_3); 1.19 (3 H, s, CH_3); 1.22 (3 H, s, CH_3); 1.33 (6 H, s, $2CH_3$); 1.47 (3 H, s, CH_3); 1.87 (3 H, s, CH_3); 4.85 (1 H, d, ^3J = 6 Hz, anomeric proton of D-xylopyranose); 5.12 (1 H, d, ^3J = 7 Hz, anomeric proton of L-arabinopyranose).

Cyclosiversioside E (VI) from (I). Progenin (VI) (190 mg), $C_{40}H_{66}O_{13}$, mp 218-220°C (from methanol), $[\alpha]_D^{21}$ +24±2° (*c* 1.0 ; chloroform–methanol, (1:1). From its IR and PMR spectra and GLC and TLC behavior, glycoside (VI) was identified as cyclosiversioside E [12].

Cyclosiversigenin (II) and Cyclosiversigenin 3-O-β-D-Xylopyranoside (IV) from (V). A solution of 75 mg of the progenin (V) in 25 ml of methanol containing 0.25% of sulfuric acid was boiled for 1.5 h, the course of hydrolysis being checked by TLC every 20 min. The reaction mixture was diluted with water to a volume of 150 ml and was shaken with butanol (4 × 30 ml). The butanolic extract was washed with water, and the solvent was distilled off. The residue was chromatographed on a column, with elution by system 6. This gave 19 mg of cyclosiversigenin (II), mp 239-241°C (from methanol), $[\alpha]_D^{23}$ + 52,7 ± 2° (*c* 1.1 ; methanol).

Further elution of the column with the same system led to the isolation of 23 mg of a glycoside with mp 263-264°C (from methanol), $[\alpha]_D^{21}$ +42±2° (*c* 0.65; methanol). The product was identified as progenin (IV) by, *inter alia*, the characteristics of its IR and PMR spectra and R_f values on TLC (systems 5 and 6) [13].

Smith Degradation of Askendoside D. A solution of 1.4 g of sodium periodate in 50 ml of water was added to 360 mg of askendoside D (I) in 100 ml of methanol, and the mixture was left at room temperature for 24 h. Then it was diluted with 150 ml of water, and 5 ml of ethylene glycol was added to the solution to decompose the excess of oxidant. The methanol was evaporated off and the reaction products were extracted with butanol. The butanolic extract was washed with water and evaporated to dryness. The residue was dissolved in 30 ml of methanol, and then 40 ml of water and 1.5 g of sodium tetrahydroborate were added and the mixture was heated on the water bath for 10 h. After cooling, 70 ml of a 1.5% aqueous methanolic (1:1) solution of sulfuric acid was added to the reaction mixture and it was left at room temperature for 48 h. Then it was diluted with a twofold volume of water, the methanol was evaporated off, and the reaction products were extracted with chloroform. The extract obtained was washed with water, dried over anhydrous sodium sulfate, and evaporated. The residue was chromatographed on a column with elution by ethyl acetate. This gave 127 mg of cyclosiversigenin (II), mp 239-241°C (from methanol), $[\alpha]_D^{29}$ + 54,5 ± 2° (*c* 1,6; methanol).

SUMMARY

A new glycoside — askendoside D — has been isolated from the roots of the plant *Astragalus taschkendicus* Bge.; it is 20S,24R-epoxycycloartane-3β,6α,16β,25-tetraol [= cyclosiversigenin] 3-O-[O-α-L-arabinopyranosyl-(1 → 2)-β-D-xylopyranoside] 6-O-β-D-xylopyranoside.

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CATALYTIC REARRANGEMENT OF A 20(S),24(R)-EPOXYDAMMARANE-3β,12α,25-TRIOL (α-D-GLUCOSE 1,2-ORTHOACETATE). II.

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The catalytic rearrangement of 20(S),24(R)-epoxydammarane-3β,12α,25-triol 3,12-di(β-D-glucose orthoacetate) leads to the formation of a complex mixture of products, predominating among which are the corresponding 12-monoglucoside and 20(S),24(R)-epoxydammar-12-ene-3β,25-diol. As compared with the rearrangement of the 20(S),24(R)-epoxydammarane-3β,12β,25-triol 3,12-diorthoester the rearrangement of the 20(S),24(R)-epoxydammarane-3β,12α,25-triol 3,12-diorthoester takes place less regioselectively, which is apparently due to the strength of an intramolecular hydrogen bond. The results of IR, PMR, and ^{13}C NMR spectroscopy for the compounds newly obtained are given.

Continuing a study of the influence of intramolecular hydrogen bonds (intraHBs) on the regiochemistry of the catalytic rearrangements of orthoesters of polyhydric polycyclic alcohols [1], we have effected the synthesis and catalytic transformation of 20(S),24(R)-epoxydammarane-3β,12α-25-triol 3,12-di(3',4',6'-tri-O-acetyl-α-D-glucopyranose orthoacetate) (II). The catalytic isomerization of the 3β,12β-diorthoester (X) under conditions given previously [2] lead, as was shown in [1], to the formation of a mixture of the 12-monoglucoside (XI) and the 12,25-diglucoside (XII).

The anomalous regioselectivity of the catalytic rearrangement of (X) is apparently due to the influence of a strong intraHB between the protons of the hydroxy group at C^{25} and the alkoxyl carbon atom of the orthoester (OE) grouping at C^{12}.

In the light of the idea of the decisive role of an intraHB in the positional directivity of the rearrangement of the 3β,12β-diorthoester (X) put forward in [1], particular interest was presented by the results of the rearrangement of the 3β,12α-diorthoester (II), since the intraHB between the proton of the hydroxy group at C^{25} and the alkoxyl oxygen atom of the OE grouping at C^{12} in (II) is considerably weaker than in (X).

Unfortunately, in the IR spectroscopy of organic compounds there is no strict quantitative relationship between the integral intensity of the absorption bands of the vibrations of a O–H...O bond in the 3300-3600 cm^{-1} region and the energy of an intraHB, and therefore

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