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TRITERPENE GLYCOSIDES OF *Astragalus* AND THEIR GENINS.

XVII. CYCLOASGENIN B FROM *Astragalus tashkendicus*

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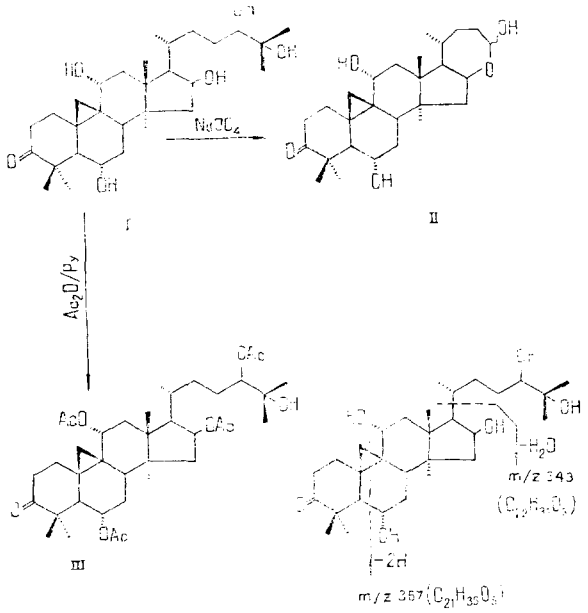
UDC 547.918:547.926

The roots of *Astragalus tashkendicus* Bge. have yielded a new triterpenoid — cycloasgenin B — the structure of which has been established on the basis of chemical transformations and spectral characteristics as (24R)-6α,11α,16β,24,25-pentahydroxycycloartan-3-one.

We are continuing the study of the methylsteroids of *Astragalus taskhendicus* Bge. (*Leguminosae*). The present paper is devoted to a proof of the structure of substance B [1], which we have called cycloasgenin B (I, scheme) [2]



The elementary composition of the genin (I), $C_{30}H_{50}O_6$, and the presence of its PMR spectrum of two one-proton doublets at 0.59 and 1.75 ppm interacting with one another in the manner of an AB system and also of the signals of seven methyl groups, permitted us to assign the compound under consideration to the methylsteroids of the cycloartane series [3].

The IR spectrum of cycloasgenin B showed carbonyl absorption at 1697 cm^{-1}, which is characteristic for a six-membered cyclic ketone. This was also shown by a signal of 21.96 ppm in the ^{13}C NMR spectrum.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 732-735, November-December, 1984. Original article submitted February 27, 1984.

0009-3130/84/2006-0691$08.50

The Cotton effect on the CD curve of cycloasgenin B (I) corresponded in magnitude and sign [$\Delta\varepsilon$ = −0.04 (318 nm); $\Delta\varepsilon$ = +1.03 (290 nm)] to the analogous indices of cycloasgenin A [1]. On this basis, it was possible to assume that compound (I), like cycloasgenin A, had a keto function at C-3 and a secondary hydroxy group in the 6α position. In actual fact, the signal of one of the methyl groups in the PMR spectrum of cycloasgenin B taken in pyridine was shifted downfield under the influence of the 6α-hydroxy function and appeared at 1.84 ppm [1, 4-6].

Taking into account what has been said above, it followed from the elementary composition of the genin (I), $C_{30}H_{50}O_6$, that its side chain had an acyclic structure.

In the PMR spectrum of compound (I) there were the signals of only four protons geminal to hydroxyl groups, at 3.81, 3.88, 4.38, and 4.75 ppm. In the PMR spectrum of its tetraacetate (III), these signals had shifted downfield and were located at 4.71, 4.78, 5.11, and 5.32 ppm, respectively. The presence of hydroxy absorption in the IR spectrum of the tetraacetate (III), and also the characteristics of the PMR spectra permitted the conclusion that the cycloasgenin B (I) molecule contained a tertiary hydroxy group. The only possible position for this group was C_{25}, since the protons of only one methyl group (CH_3-21) resonated in the form of a doublet at 1.12 ppm.

Cycloasgenin B (I) was oxidized with sodium periodate. Consequently, the genin (I) contained an α-diol grouping. The periodate oxidation of cycloasgenin B gave a product (II) with a molecular weight of 446, the structure of which will be discussed below. The loss of 60 mass units on passing from the genin (I) to the product (II) unambiguously determined the position of the glycol grouping at C-24—C-25.

The absolute configuration of the C-24 chiral center was calculated by comparing the ^{13}C NMR spectra of cycloasgenins B and C [5]. In the ^{13}C NMR spectrum of cycloasgenin C, the C-24 atom, having the R configuration, resonates at 80.52 ppm. The signal of the same carbon atom in the spectrum of cycloasgenin B was observed at 80.46 ppm. The good agreement of the chemical shifts of the asymmetric carbon atom under consideration showed that cycloasgenin B also had the 24R absolute configuration.

The mass spectrum of cycloasgenin B showed the peaks of ions with m/z 367 ($C_{21}H_{35}O_5$) and 343 ($C_{22}H_{31}O_3$), which are characteristic for the cycloartanes [7, 8]. The first of them was formed by the cleavage of the C-5—C-6, C-9—C-10, and C-9—C-19 bonds and the migration of two hydrogen atoms. The second ion arose as the result of the cleavage of the C-17—C-20 bond and the elimination of one molecule of water. These ions showed that the two remaining unidentified hydroxy groups must be present in rings C and D. Their positions were determined in the following way.

In the PMR spectrum of cycloasgenin B taken in pyridine, just as in the spectrum of cycloasgenin A [1], one of the cyclopropane protons underwent a considerable paramagnetic shift and resonated at 1.75 ppm. This fact determined the position of the hydroxy group in ring C at C-11.

The proton geminal to this hydroxyl resonated at 4.38 ppm in the form of a quartet with the spin—spin coupling constants $^3J_1$ = 9.3 and $^3J_2$ = 3.4 Hz. The values given agree with those for the PMR spectrum of cycloasgenin A. This means that in cycloasgenin B, as well, the hydroxy group at C-11 had the α orientation.

The proton geminal to the hydroxy group located in ring D resonated at 4.75 ppm in the form of a quartet with a distribution of the line intensities as 1:3:3:1 and with Σ^3J = 20.2 Hz. These characteristics correspond to hydrogen atoms interacting vicinally with three protons with close values of ^3J. The good agreement of the magnitudes given with the analogous indices of the spectra of cycloasgenin A and cycloasgenin C showed that cycloasgenin B contained a 16β-hydroxy group.

It must be mentioned that in the PMR spectrum of product (II) obtained as the result of the periodate oxidation of the genin (I) no signal of the proton of an aldehyde group was observed. This was explained by the fact that the C-24 aldehyde group formed a semiacetal with the hydroxy group at C-16. We have previously observed the formation of such a product in the periodate oxidation of cycloasgenin C [5]. We may point out only the identity of the chemical shifts of the H-16 atom (4.22 ppm) and the H-24 atom (4.64 ppm) in the PMR spectra of compound (II) and of the analogous product obtained from cycloasgenin C. Consequently, product (II) consisted of 16β,11α,24-tri-hydroxy-16β,24ξ-epoxy-25-norcycloartan-3-one.

The experimental facts given permit the conclusion that cycloasgenin B is (24R)-6α,11α, 16β,24,25-pentahydroxycycloartan-3-one.

EXPERIMENTAL

General observation see [1]. The following solvent systems were used: 1) benzene—ethyl acetate (3:1); 2) chloroform—methanol (10:1).

PMR spectra were taken at 300 MHz in deuteropyridine or deuterochloroform (δ, 0 — TMS), and ^{13}C NMR spectra on a CFT-20 instrument (Varian) in pyridine (δ, 0 — TMS).

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

Cycloasgenin B (I) — substance B [1], $C_{30}H_{50}O_6$, mp 232-233°C (from methanol, $[\alpha]_D^{27}$ +98.9 ± 2 (c 0.89; methanol). ν_{max}^{KBr}, cm^{-1}: 35 0*-3330 (OH); 3060 (CH_2 of a cyclopropane ring); 1697 (C=O at C-3). CD (c 0.1 methanol): $\Delta\varepsilon$ = −0.04 (318 nm); $\Delta\varepsilon$ = +1.03 (290 nm). Mass spectrum, m/z (%): M^+ 506 (4.4), 488 (39.1), 470 (13.0), 455 (8.7), 452 (10.9), 437 (8.7), 411 (13.0), 393 (13.0), 367 (100), 351 (52.2), 343 (13.0), 331 (17.4), 325 (21.7). PMR (C_5D_5N), δ, ppm: 0.59 (1 H, at C-19, d, ^2J = 4.3 Hz); 1.75 (1 H at C-19, d, ^2J = 4.3 Hz); 1.12 (3H at C-21, d, ^3J = 6.6 Hz); 1.00, 1.51, 1.53, 1.55, 1.56, and 1.84 (3 H each, s, CH_3 groups); 3.81 (1 H, q, $^3J_1$ = 10.4 and $^3J_2$ = 2.3 Hz, H-24); 3.88 (1 H, sx, $^3J_1$ = $^3J_2$ = 10.0 and $^3J_3$ = 3.2 Hz, H-6); 4.38 (1 H, q, $^3J_1$ = 9.3 and $^3J_2$ = 3.4, H-11); 4.75 (1 H, q, Σ^3J = 20.2 Hz, H-16).

Cycloasgenin B Tetraacetate (III) from (I). Cycloasgenin B (12 mg) was acetylated with 0.15 ml of acetic anhydride in 0.25 ml of pyridine at room temperature for 24 h. After the solvents had been distilled off, the residue was chromatographed on a column with elution by system 1. This gave 10 mg of the amorphous tetraacetate (III), $C_{38}H_{58}O_{10}$, $[\alpha]_D^{20}$ +153.3 ± 2° (c 0.3; methanol). ν_{max}^{KBr}, cm^{-1}: 3565-3405 (OH); 1745-1705, 1250 (C=O at C-3 and ester groups). Mass spectrum, m/z (%): M^+ 674 (1.9), 656 (0.5), 614 (3.3), 596 (1.0), 572 (13.6), 554 (29.5), 512 (15.9), 494 (54.5), 434 (29.5), 419 (15.9), 391 (13.6), 325 (21.6), 307 (100). PMR ($CDCl_3$), δ, ppm: 0.76 (1 H at C-19, d, ^2J = 5.8 Hz); 0.86 (1 H at C-19, d, ^2J = 5.8 Hz); 0.91 (3 H at C-21, d, ^3J = 6.5 Hz); 0.94, 1.04, 1.15, 1.17, 1.18, 1.19 (3 H each, s, CH_3 groups); 2.02, 2.03, 2.04, 2.09 (3 H each, s, CH_3's of acetyl groups); 4.71 (1 H, q, $^3J_1$ = 10.6 and $^3J_2$ = 2.3 Hz, H-24); 4.78 (1 H, sx, Σ^3J = 20.2 Hz, H-6); 5.11 (1 H, q, $^3J_1$ = 6.8 and $^3J_2$ = 2.3 Hz, H-11); 5.32 (1 H, sx, Σ^3J = 21.0 Hz, H-16).

6α,11α,24-Trihydroxy-16β,24ξ-epoxy-25-norcycloartan-3-one (II) from (I). To 16 mg of cycloasgenin B (I) in 2 ml of ethanol was added 30 mg of sodium periodate in 0.5 ml of water, and the mixture was left at room temperature for 10 h. A few drips of ethylene glycol was added to the reaction mixture to decompose the excess of oxidizing agent, and it was diluted with water to a volume of 15 ml and was extracted with chloroform. The chloroform extract was evaporated and the residue was chromatographed on a column with elution by system 2. This gave 9 mg of product (II), $C_{27}H_{42}O_5$, mp 135-140°C (from system 2), $[\alpha]_D^{20}$ +106.6 ± 2° (c 0.6; methanol), ν_{max}^{KBr}, cm^{-1}: 3520-3345 (OH); 1704 (C=O at C-3). Mass spectrum, m/z (%): M^+ 446 (6.3), 428 (62.5), 410 (50.0), 382 (18.8), 367 (12.5), 343 (25.0), 339 (18.8), 325 (34.4), 307 (100), 291 (87.5), 289 (56.3), 278 (31.3), 273 (62.5). PMR ($CDCl_3$), δ, ppm: 0.48 (1 H at C-19, d, ^2J = 4.8 Hz); 0.98 (3 H at C-21, d, ^3J = 6 Hz); 0.88, 1.18, 1.25, 1.35 (3 H each, s, CH_3 groups); 3.65 (1 H, br.m, H-6); 3.97 (1 H, br.m, H-11); 4.22 (1 H, q, Σ^3J = 23.2 Hz, H-16); 4.64 (1 H, br.m, H-24).

SUMMARY

A new triterpene ketone has been isolated from the roots of *Astragalus tashkendicus* Bge. — cycloasgenin B — which has the structure of (24R)-6α,11α,16β,24,25-pentahydroxycycloartan-3-one.

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TRANSFORMED STEROIDS.

141. IODOSOBENZENE DIACETATE FOR THE α-HYDROXYLATION OF [17,16a]-2'-METHYLOXAZOLINE DERIVATIVES OF 20-KETOSTEROIDS

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UDC 542.91:547.92

Using the [17,16a-d]-2'-methyloxazoline derivatives of 3β-hydroxypregn-5-en-20-one (I) as an example, the α-hydroxylation reaction has been studied with the use of rodosobenzene diacetate in a methanolic solution of NaOH as the α-hydroxylating reagent. The reaction took place successfully through the stage of the formation and isolation of the corresponding [17,16a-d]-2'-methyloxazoline derivative of 20, 20-dimethylpregn-15-ene-3β,21-diol (II), the dimethyl acetal protection of which was eliminated by acid hydrolysis in methanol. The results of physicochemical investigations and biological trials of the [17,16a-d]-2'-methyloxazoline derivatives of 21-hydroxy-21-acetoxy-20-ketosteroids obtained are given.

The hydroxylation of position 21 of 16,17-substituted steroids is a complex task which sometimes cannot be resolved by ordinary methods. Iodosobenzene diacetate (IBD) has recently been proposed as a 21-hydroxylating reagent for 3β-hydroxypregn-5-en-20-one [1]. We have used this reagent successfully in the reaction with the [17,16a-d]-2'-methyloxazoline derivatives of 3β-hydroxypegn-5-en-20-one (I), after the methods of constructing the corticoid side chain usually used has proved unsuccessful.

The reaction of (I) with IBD in methanolic NaOH solution at 20°C took place through the formation of the 20-(dimethyl acetal) (II), the acetal group in which was eliminated by acid (HCl) hydrolysis in methanol, giving the 21-hydroxy derivative of the [17,16a-d]-2'-methyloxazoline compound (IV). The selective acetylation of the 21-hydroxy group of (IV) with acetic anhydride in pyridine at a low temperature (−30°C) gave the 21-acetoxy derivative (V), which was oxidized by the Oppenhauer method to the Δ^4-3-ketone (VI). The latter was converted by alkali ($KHCO_3$) saponification in methanolic solution into the 2-hydroxy-Δ^4-3-ketone (VII), which cannot be obtained by the selective oxidation of the diol (IV).

The structures of the products obtained were shown by a combination of physicochemical methods. The mass spectra of all the compounds represented in the scheme had molecular peaks. Arguments in favor of the presence of a methyloxazoline ring in each of compounds (II-VII) are the characteristic absorption of the C=N band at ν 1650-1670 cm^{-1} observed in the IR spectra, and the resonance signal of the methyl group in an oxazoline ring δ 1.85-1.92 ppm in the PMR spectra. The fact, not without interest, of the splitting of the carbonyl band in the IR spectrum of (IV) with ν 1700 and 1720 cm^{-1} is apparently due to the formation of an intramolecular hydrogen bond with the 21-hydroxy group. It follows from the PMR spectra that the protons of the 21-methylene group for each of the products obtained are either chemically equivalent (compounds (II), (V), and (VI)) or nonequivalent (compounds (III), (IV), and (VII)). In the latter case they exhibit the geminal coupling that is characteristic for

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Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 736-738, November-December, 1984. Original article submitted November 10, 1983.

 0009-3130/84/2006-0694$08.50