TRITERPENE GLYCOSIDES OF Astragalus AND THEIR GENINS.

XXXI. CYCLOORBIGENIN B FROM Astragalus orbiculatus

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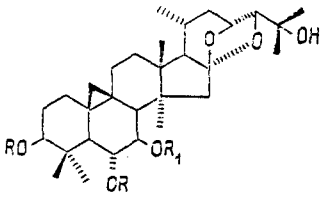
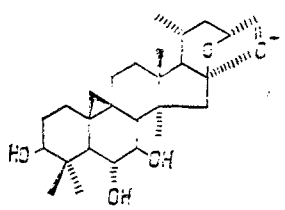
A new methylsteroid of the cycloartane series has been isolated from the epigeal part of Astragalus orbiculatus Ledeb. (Leguminosae); it has the structure of a (23R,24S)-16β,23; 16α,24-diepoxycycloartane-3β,6α,25-tetraol.

Continuing a study of the cycloartane methylsteroids of plants of the genus Astragalus, from the epigeal part of Astragalus orbiculatus Lebed. (Leguminosae) we have isolated substance 2 [1] of glycosidic nature. The acid hydrolysis of glycoside 2 gave a new methylsteroid which we have called cycloorbigenin B (I). In the present paper we consider its structure.

The elementary composition of genin (I), $C_{30}H_{48}O_6$, the presence of its PMR spectrum of two one-proton doublets of an AB system at 0.28 and 0.64 ppm characteristic for an isolated cyclopropane methylene, and the signals of seven methyl groups indicated that the compound under consideration belonged to the cycloartane series [2]. The IR spectrum of cycloorbigenin B, containing an absorption band at 3045 cm^{-1}, also agreed with this conclusion.



I. $R = R_1 = H$
II. $R = Ac$, $R_1 = H$
III. $R = R_1 = Ac$



m/z 445 ($C_{27}H_{41}O_5$)

In the mass spectrum on genin (I), the 100% peak was that of an ion with m/z 445 ($M^+ - 59$). On this basis, it may be assumed that the molecule of (I) contains a hydroxyisopropyl fragment readily eliminated under electron impact. We have observed an analogous process for cycloorbigenin [3].

In the PMR spectrum of genin (I), in addition to the above-mentioned signals, another pair of one-proton doublets of an AB system was observed at 2.46 and 2.70 ppm, which were assigned to the isolated C-15 methylene group. It was also easy to assign a one-proton singlet at 3.60 ppm to H-24 and a three-proton doublet at 0.76 ppm to CH_3-21 [3]. The facts given indicate that the side chain of the new genin was identical with that of cycloorbigenin.

Thus, the three oxygen atoms remaining unidentified were represented by hydroxylic functions.

The acetylation of genin (I) with acetic anhydride in pyridine gave a diacetate (II) and a triacetate (III). A consideration of the PMR spectra of the acetates (II) and (III) showed the secondary nature of all the hydroxy groups present in the polycyclic part of the molecule. The position of one of them followed from the PMR spectrum of genin (I) taken in deuteropyridine, where the signal of the 4α-methyl group was observed at 1.8 ppm and indicated the presence of 6α-hydroxy group [2].

In the PMR spectrum of the diacetate (II) the signals of two protons geminal to the acetoxy groups were shifted downfield and appeared at 4.68 and 5.04 ppm. The latter con-

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TABLE 1. Chemical Shifts of the Protons of Cycloorbigenin B (I) and Its Derivatives (δ, ppm, 0 – HMDS)

Compound	Positions of the protons				
	H-3	H-6	H-7	2H-15	2H-19
I	3,46—3,66	3,46 - 3,66	3.46—3,66	2,46; 2,70d ^2J=14 Hz	0,28; 0,64 d ^2J=4 Hz
II	5,04dd ^3J=12; 8Hz	4,68m	3,62t ^3J=8 Hz	2,40; 2,54d ^2J=14 Hz	0,20; 0,62 d ^2J=4 Hz
III	5,04m*	4,60t** ^3J=8Hz	5,04*t ^3J=8Hz	2,02; 2,24d ^2J=14Hz	0,22; 0,62 d ^2J=4 Hz

Compound	Positions of the protons			
	H-23	H-24	CH_3 groups	OAc
I	4,66	3,60 s	0,76d (^3J=6 Hz); 1,12; 1,26; 1,28; 1,35 (2×CH_3) 1,80	—
II	4,56	3,54s	0,72d (^3J=6 Hz); 0,92; 1,02; 1,08; 1,23 (2×CH_3) 1,34	1,92; 1,94
III	4,60** m	3,54s	0,74 d (^3J=6Hz); 0,80; 0,96; 1,00; 1,20; 1,24 1,30	1,90; 1,92; 1,98

sisted of a doublet of doublets with the SSCCs $^3J_1$ = 12 Hz and $^3J_2$ = 8 Hz. This signal must be assigned to 3α-H. Consequently, one of the secondary hydroxyls is located at C-3 and has the β-orientation. The chemical shift of the C-3 atom, (78.05 ppm) in the ^{13}C NMR spectrum confirmed the correctness of this conclusion.

In the PMR spectrum of the diacetate (II) taken in deuterochloroform, the signal of the 4α-methyl group had undergone an upfield shift and, consequently, the second acetyl group was located at C-6 and the multiplet at 4.68 ppm related to H-6. In the spectrum of the triacetate (III), H-6 and an unidentified proton geminal to an acetoxy group resonated at 4.60 and 5.04 ppm in the form of triplets with ^3J = 8 Hz. The triplet nature of the splitting of the H-6 signal showed that it was part of an α-glycol system, which means that the third secondary hydroxy group must be located at C-7 and have the β-orientation. In actual fact, substance (II) was oxidized by sodium periodate, which confirmed the conclusion of the presence of an α-diol grouping in the molecule.

Thus, cycloorbigenin B has the structure of (23R,24S)-16β,23; 16α,24-diepoxycycloartane-3β,6α,7β,25-tetraol.

EXPERIMENTAL

For general observations see [3]. PMR spectra were taken on a XL-200 (Varian) spectrometer, and ^{13}C NMR spectra on a AH-400 (Bruker) instrument in deuteropyridine.

Cycloorbigenin B (I). The fractions containing substance 2 obtained in the separation of the triterpenoids from Astragalus orbiculatus [1] were chromatographed repeatedly on a column with elution by the chloroform–methanol–water (70:21:1) system. In this way, 500 mg (0.008% on the weight of the air-dry raw material) of glycoside 2 was isolated. A solution of 250 mg of this substance in 25 ml of methanol containing 0.25% of sulfuric acid was heated at 50-60°C for 24 h and was then diluted with water and the methanol was evaporated off. The reaction products were extracted with chloroform and the chloroform extract was washed with water and evaporated to dryness. The residue was chromatographed on column with elution with the chloroform–methanol (20:1) system. The fractions containing genin (I) were accumulated. Recrystallization from benzene–methanol (10:1) yielded 130 mg of cycloorbigenin B, $C_{30}H_{48}O_6$, mp 201-203°C, $[\alpha]_D^{29}$ + 20.7 ± 2° (c 0.77; methanol), ν_{max}^{KBr}, cm^{-1}: 3580-3225 (OH), 3045 (CH_2 of a cyclopropane ring). Mass spectrum, m/z (%): M^+ 504 (0.63), 489 (2.2), 486 (1.2), 471 (1.1), 468 (1.4), 453 (0.9), 445 (100), 427 (6.0), 416 (2.1), 409 (3.0), 389 (8.6), 347 (6.8), 287 (2.7), 269 (2.7). ^{13}C NMR spectrum (δ, ppm, 0 – TMS): 78.05 (C-3), 72.88 (C-6), 75.00 (C-7).

The 3,6,7-Triacetate (III) and 3,6-Diacetate (II) of Cycloorbigenin B from (I). Cycloorbigenin B (I) (25 mg) was acetylated with 2 ml of acetic anhydride in 2 ml of absolute pyridine at room temperature for 48 h. The residue after the solvents had been evaporated off was chromatographed on a column with elution by chloroform. This yielded 6 mg of the triacetate (III), $C_{36}H_{54}O_9$, mp 257-259°C (from chloroform–hexane), $[\alpha]_D^{27}$ +21.5 ± 2° (c 0.38; benzene). ν_{max}^{KBr}, cm^{-1}. 3490 (CH_2 of a cyclopropane ring), 1750, 1720, 1260 (ester groups). Mass spectrum, m/z (%): M^+ 630 (0.8), 615 (5.4), 597 (1.4), 571 (38.4), 555 (30.7), 529 (11.6), 510 (84.6), 495 (19.9), 469 (14.5), 451 (100), 437 (17.2), 435 (19.9), 409 (15.3), 391 (24.4), 370 (11.7), 311 (11.7).

Continued elution of the column with chloroform led to the isolation of 11 mg of the amorphous diacetate (II), $C_{34}H_{52}O_8$, $[\alpha]_D^{30}$ +30 ± 2° (c 0.1; methanol), ν_{max}^{KBr}, cm^{-1}; 3580-3355 (OH), 1740, 1250 (ester groups). Mass spectrum, m/z (%): M^+ 588 (1.0), 573 (2.8), 529 (100), 513 (7.5), 500 (3.3), 499 (3.1), 473 (8.7), 469 (25), 468 (8.7), 453 (8.7), 451 (13.7), 439 (8.7), 409 (12.5), 269 (9.3), 171 (8.7).

Periodate Oxidation of Cycloorbigenin B. To 5 mg of genin (I) in 2 ml of methanol was added 20 mg of sodium periodate in 3 ml of water, and the mixture was left at room temperature for 30 min. Thin-layer chromatography of the reaction mixture in the chloroform–methanol (15:1) system in comparison with a sample of the initial substance showed that the genin (I) had been oxidized completely.

SUMMARY

A new cycloartane methylsteroid – cycloorbigenin B, which has the structure of (23R,24S)-16β,23; 16α,24-diepoxycycloartane-3β,6α,7β, 25-tetraol – has been isolated from the epigeal part of Astragalus orbiculatus Ledeb. (Leguminosae).

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GLYCOSYLATION OF TRITERPENOIDS OF THE DAMMARANE SERIES. X. REGIO- AND STEREOSELECTIVE SYNTHESIS OF 20(S)-PROTOPANAXADIOL 3-O-β-D-GLUCOPYRANOSIDE (GINSENOSIDE Rh_2)

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The regio- and stereoselective synthesis of ginsenoside Rh_2, which possesses antitumoral activity, has been effected by the glycosylation of 12β-acetoxydammar-24-ene-3β,20(S)-diol. Condensation with α-acetobromoglucose was carried out in the presence of silver oxide in dichloroethane at room temperature, and the yield of the desired glycoside amounted to 50%. A method for the selective protection of the C-12-OH group of dammar-24-ene-3β,12β,20(S)-triol [20(S)-protopanaxadiol] has been proposed.

20(S)-Protopanaxadiol 3-O-β-D-glucopyranoside (ginsenoside Rh_2) (1), which possesses antitumoral activity [1, 2] has been obtained by Japanese workers as the result of the partial hydrolysis of ginseng glycosides (ginsenosides Rb_1, Rb_2, Rb_3, Rc, and Rd [3], the aglycon of which is 20(S)-protopanaxasiol [dammar-24-ene-3β,12β,20(S)-triol or 3-epibetulafolienetriol] (2). We have sinthesized this compound together with four other glycosides by the condensation of the triol (2) with α-acetobromoglucose [4]. However, the absence of regio-

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