TRITERPENE GLYCOSIDES OF Astragalus AND THEIR GENINS

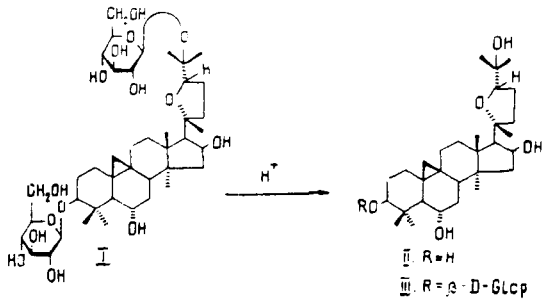
XXXIV. CYCLOARALOSIDE E FROM Astragalus amarus

M. I. Isaev and N. K. Abubakirov

UDC 547.918:547.926

Five compounds of glycosidic nature, designated 5-9 have been isolated from the roots of the plant Astragalus amarus Pall. (Leguminosae). The structure of substance 8, which has been called cycloaraloside E, has been shown on the basis of chemical transformations and spectral characteristics. Cycloaraloside E is 20R, 24S-epoxycycloartane-3β,6α,16β,25-tetraol 3,25-di-O-β-D-glucopyranoside.

We are continuing the study of the triterpenoids of the plant Astragalus amarus Pall. (Leguminosae) [1]. From the roots of this plant, we have isolated another five substances of glycosidic nature which have been designated in order of increasing polarity as substances 5-9. The present paper is devoted to the establishment of the structure of substance 8, which we have called cycloaraloside E (I).



The PMR spectrum of glycoside (I), containing at 0.08 and 0.42 ppm one-proton doublets of a AB system and also the signals of seven methyl groups in the strong field, permitted the compound under consideration to be assigned to the triterpenoids of the cycloartane series [2, 3]. In actual fact, acid hydrolysis of cycloaraloside E gave a genin which was identified as cyclosieversigenin (II) [3]. D-Glucose was detected in the hydrolysate by TLC and PC. It was found by GLC [4] that glycoside (I) contained two D-glucose residues. This conclusion was also confirmed by the ^{1}H and ^{13}C NMR spectra in which the signals of two anomeric protons, at 4.82 and 4.90 ppm, and of two anomeric carbon atoms, at 106.95 and 98.70 ppm, could readily be traced.

The signals of the anomeric protons of the D-glucose residues in the PMR spectrum were observed in the form of doublets with the SSCCs ^{3}J = 7-8 Hz, which showed the β-configurations of the glycosidic bonds and the C1 conformation and the pyranose form of both monosaccharide residues. Confirmation of this were the formation of cycloaraloside A (III) on the partial hydrolysis of glycoside (I) and the ^{13}C NMR spectrum of the latter (Table 1). The chemical shift of the anomeric carbon atom of the second D-glucose residue (98.70 ppm) showed that it was attached to a tertiary hydroxy group. As was to be expected, from a comparative analysis of the ^{13}C NMR spectra of compounds (I-III) it followed that in the molecule of cycloaraloside E the C-3 and C-25 atoms had undergone a glycosylation effect, their resonance lines being observed at 88.95 and 78.45 ppm, respectively.

Thus, we are justified in concluding that cycloaraloside E has the structure of 20R,24S-epoxycycloartane-3β,6α,16β,25-tetraol 3,25-di-O-β-D-glucopyranoside.

Institute of Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 656-659, September-October, 1990. Original article submitted January 2, 1990.

0009-3130/90/2605-0559$12.50

TABLE 1. Chemical Shifts of the Carbon Atoms of Compounds (I-III) (C_5D_5N, δ, ppm, O– TMS)

C atom	Compound			C atom	Compound		
	I	II	III		I	II	III
1	32,40	32,72	32,41	23	25,80	26,29[a]	26,37[a]
2	30,0	31,30	30,16	24	82,05	81,57	81,64
3	88,95	78,21	88,96	25	78,45[b]	71,19	71,26
4	42,60	42,28	42,58	26	22,80*	27,04*	27,04*
5	53,85	53,86	53,93	27	25,50*	28,09	28,53*
6	68,10	68,27	67,97	28	19,95	20,17	20,09
7	38,55	38,69	38,54	29	28,65	29,28	28,91
8	46,95	47,21	47,06	30	16,50	16,16	16,66
9	20,70	20,84	20,84		residue 3-O-β-*D*-Glcp		
10	29,25	29,80	29,50	1	106,95		106,82
11	26,10	26,29[a]	26,37[a]	2	75,75		75,82
12	33,45	33,31	33,31	3	78,45[b]		78,66
13	45,15	44,89	44,97	4	71,85		71,78
14	46,05[a]	46,09	45,91	5	77,85[c]		78,06
15	46,05[a]	46,69	46,09	6	62,85		62,97
16	73,80	73,35	73,43		residue 25-O-β-*D*-Glcp		
17	58,20	58,26	58,26	1	98,70		
18	21,45	21,51	21,51	2	75,15		
19	30,45	31,0	30,55	3	78,45[b]		
20	87,15	87,17	87,17	4	71,25		
21	27,75	28,46	28,41	5	77,85[c]		
22	34,95	34,81	34,88	6	62,70		

*The signals marked by the same letters are superposed on one another. The asssignments of the signals marked by asterisks are ambiguous within a column.

EXPERIMENTAL

General Observations. The following systems of solvents were used: 1) chloroform–methanol–water (70:12:1); 2) chloroform–methanol–water (70:23:4); 3) chloroform–methanol (15:1); 4) chloroform–methanol–water (65:35:5); and 5) n-butanol–pyridine–water (6:4:3).

PC was conducted on type FN-11 paper. The conditions of GLC, TLC and CC are given in [4].

^1H and ^{13}C NMR spectra were taken on a Tesla BS-567A instrument in deuteropyridine (δ, ppm; for ^1H, O–HMDS, and for ^{13}C, O–TMS).

For the Isolation and Separation of the Isoprenoids of Astragalus armarus, see [1]. After the elimination of substances 1-4, the column was eluted successively with systems 1 and 2. Fractions containing the individual substances 5-9 were isolated. To free it from pigments, each substance was repeatedly rechromatographed, giving substances 5 (130 mg – 0.087%; here and below the yields have been calculated on the air-dry raw material), 6 (5.18 g – 0.345%), 7 (30 mg – 0.002%), 8 (180 mg – 0.012%), and 9 (1.15 g – 0.077%).

Cycloaraloside E (I), substance 8, $C_{42}H_{70}O_{15}$, mp 180-182°C (from chloroform–methanol (1:1)), $[\alpha]_D^{28}$ −5 ± 2° (c 0.82; methanol), ν_{max}^{KBr}, cm^{-1}: 3600-3240 (OH). PMR spectrum (C_5D_5N): 0.08 and 0.42 (2 H-19, d, ^2J = 4 Hz), 0.80 (CH_3, s), 1.16 (CH_3, s), 1.18 (2 × CH_3, s), 1.28 (CH_3, s), 1.52 (CH_3, s), 1.84 (CH_3, s), 4.82 (2 H, anomeric proton of a D-glucose residue at C-3, d, ^3J = 7 Hz, and H-16; the signal of the latter was masked by the signal of the anomeric proton); 4.90 (anomeric proton of a D-glucose residue at C-25, d, ^3J = 8 Hz).

Acid Hydrolysis of Cycloaraloside E (I). Glycoside (I) (50 mg) was hydrolyzed with 20 ml of 0.5% methanolic sulfuric acid at 50°C for 4 h. Then the reaction mixture was diluted with water and the methanol was evaporated off. The precipitate that deposited was filtered off and chromatographed on a column with elution by system 3. This led to the isolation of 17 mg of cyclosieversigenin (II), mp 239-241°C (from methanol) $[\alpha]_D^{27}$ +51 ± 2° (c 1.1; methanol).

The filtrate was evaporated to a volume of 15 ml and was boiled for 1 h, after which it was neutralized with ARA-8p anion-exchange resin. D-Glucose was detected in the residue by the methods of TLC in system 4 and PC in system 5 after the eliminaton of the anion-exchange resin and evaporation of the water.

Quantitative analysis of the monosaccharides of cycloaraloside E with the aid of GLC [4] in the presence of D-xylose as standard showed that the compound contained two D-glucose residues.

Cyclosieversigenin (II) and Cycloaraloside A (III) from (I). Glycoside (I) (70 mg) was hydrolyzed with 20 ml of 0.25% methanolic sulfuric acid at 50°C for 2 h. The reaction mixture was diluted with water, and the methanol was evaporated off. The precipitate that had deposited was filtered off and was chromatographed on a column with elution by system 3. This led to the isolation of 10 mg of cyclosieversigenin (II), mp 239-241°C (from methanol), $[\alpha]_D^{27}$ +51 ± 2° (c 1.0; methanol).

Continued elution of the column with system 1 gave 33 mg of a progenin (III), mp 240-242°C (from system 1), $[\alpha]_D^{27}$ +33 ± 2° (c 1.0; methanol). The PMR spectrum of glycoside (III) also coincided with that of cycloaraloside A.

LITERATURE CITED

1. M. I. Isaev, M. B. Gorovits, and N. K. Abubakirov, Khim. Prir. Soedin., 806 (1989).
2. M. I. Isaev, M. B. Gorovits, and N. K. Abubakirov, Khim. Prir. Soedin., 431 (1985).
3. M. I. Isaev, M. B. Gorovits, and N. K. Abubakirov, Khim. Prir. Soedin., 156 (1989).
4. M. A Agzamova, M. I. Isaev, M. B. Gorovits, and N. K. Abubakirov, Khim. Prir. Soedin. 719 (1986).
5. H. K. Wang, K. He, L. Ji, Y. Tezuka, T. Kikuchi, and I. Kitagawa, Chem. Pharm. Bull. 37, 2041 (1989).

SYNTHESIS, METHYLATION, AND ACYLATION OF 1,2-DIHYDRODEOXY-VASICINONES AND THEIR HOMOLOGS

Kh. M. Shakhidoyatov and G. A. Belova

UDC 547.944/945+547.856.1

2,3-Trimethylene- and 2,3-pentamethylene-1,2,3,4-tetrahydro-4-quinazolones and their 6-methyl and 6-bromo derivatives have been obtained by the reduction of deoxyvasicinone and its 6-methyl and 6-bromo derivatives and also their seven-membered homologs at the cycloalkane ring with sodium tetrahydroborate in ethanol. The alkylation and acylation reactions of the above-mentioned reducing compounds have been studied.

The results of a study of the products of the reduction of deoxyvasicinone at the C=O bond (3,4-dihydroquinazolines) are widely represented in the literature. Hitherto, inadequate attention has been devoted to derivatives of 1,2-dihydrodeoxyvasicinone, although there is information on their synthesis by sodium tetrahydroborate reduction [1].

In order to find biologically active compounds in this series, we have performed the regiospecific reduction of deoxyvasicinone and its substituted and seven-membered homologs at the cycloalkane ring. The reaction took place smoothly under the conditions described for certain substituted 4-quinazolones in [2]. As the starting materials we used deoxyvasicinone and its 6-methyl and 6-bromo derivatives (Ia-c).

The application of this reaction to the seven-membered homologs of deoxyvasicinone (IIa-c) likewise gave the products of the reduction of the C=N bond (scheme 1).

The 1,2-dihydrodeoxyvasicinones (IIIa-c) and their homologs (IVa-c) that were synthesized are well crystallizing substances soluble in many polar organic solvents (chloroform, DMFA, DMSO, and acetone) and sparingly soluble in water and neutral solvents (hexane, petroleum ether, diethyl ether).

Institute of Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent.

Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 659-663, September-October, 1990. Original article submitted December 25, 1989; revision submitted February 5, 1990.

0009-3130/90/2605-0561$12.50