TRITERPENE GLYCOSIDES AND THEIR GENINS FROM *Thalictrum foetidum*.

V. STRUCTURE OF CYCLOFOETOSIDE B

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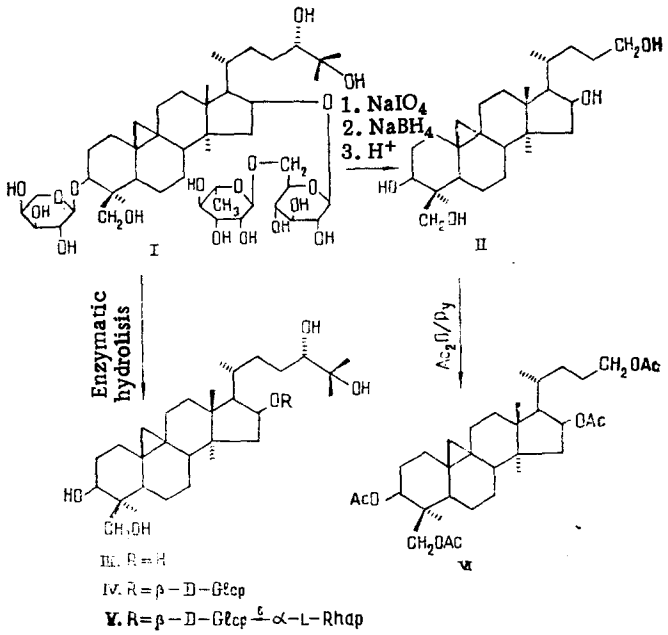
A new glycoside (cyclofoetoside B) (I) has been isolated from the epigeal part of the plant *Thalictrum foetidum* L. (Ranunculaceae). On the basis of chemical transformations and with the aid of physicochemical characteristics it has been established that cyclofoetoside B is 24S-cycloartane-3β,16β,24,25,29-pentaol 3-O-α-L-arabinopyranoside 16-O-[O-α-L-rhamnopyranoside-(1 → 6)-β-D-glucopyranoside], $C_{47}H_{80}O_{17}$, mp 194-197°C (methanol); $[\alpha]_D^{24}$ +15.7 ± 2° (c 0.88; pyridine). The enzymatic hydrolysis of (I) has yielded cyclofoetigenin B (III), 24S-cycloartane-3β,16β,24,25,29-pentaol 16-O-β-D-glucopyranoside, (IV), $C_{36}H_{62}O_{10}$, mp 223-225°C (acetone), $[\alpha]_D^{24}$ +37 ± 2° (c 0.97; methanol) and 24S-cycloartane-3β,16β,24,25,29-pentaol 16-O-[O-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside, $C_{42}H_{72}O_{14}$, mp 229-231°C (methanol), $[\alpha]_D^{30}$ +41 ± 2° (c 0.7; methanol). Details of the IR and ^1H and ^{13}C NMR spectra of the compounds are given.

The present paper is devoted to a determination of the structure of glycoside B, which we have isolated from the epigeal part of *Thalictrum foetidum* L. (Ranunculaceae) [1] and have called cyclofoetoside B (I, scheme).



It has been shown previously that glycoside (I) belongs to the cycloartane series and the genin of this glycoside is cyclofoetigenin B (III) [2].

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According to GLC results [3], cyclofoetoside B contains D-glucose, L-arabinose, and L-rhamnose residues in a ratio of 1:1:1. The Smith degradation [4] of glycoside (I) led to the tetraol (II) with M^+ 434, which is 58 mass units smaller than the molecular weight of cyclofoetigenin B (M^+ 492). This fact shows the cleavage of a C-24–C-25 α-glycol grouping. A comparison of the PMR spectra of the nor- compound (II) and of its tetraacetate (VI) showed that substance (II) had two secondary (at C-3 and C-16) and two primary (at C-24 and C-30) hydroxy groups. Consequently, compound (II) was 25-norcycloartane-3β,16β,24,30-tetraol. An analogous derivative has been obtained from cyclofoetoside A [5].

The formation of the tetraol (II) showed that the hydroxy group at C-16 of the genin in glycoside (I) was linked with a sugar residue.

The enzymatic hydrolysis (with the gastric juice of the grape snail) of cyclofoetoside B gave cyclofoetigenin B (III) and the progenins (IV) and (V).

GLC showed that progenin (IV) contained one D-glucose residue and progenin (V) D-glucose and L-rhamnose residues in a ratio of 1:1.

A comparative analysis of the ^{13}C NMR spectra of cyclofoetigenin B (III) and the progenin (IV) (Table 1) showed that the C-16 atom experienced a glycosylation effect ($\Delta\delta$ = +10.5 ppm). On passing from the monoside (IV) to the bioside (V) no appreciable changes were observed in the chemical shifts of the carbon atoms of the genin moiety. Only the signal of the C-6 atom of the D-glucose residue underwent a paramagnetic shift ($\Delta\delta$ = +5.1 ppm). This shows the position of the L-rhamnose residue at C-6 of the D-glucose residue.

It follows from a comparison of the spectra of glycosides (I) and (V) that a L-arabinose residue was attached at C-3 of the genin, since the signal of this carbon atom in cyclofoetoside B (I) was shifted downfield by 9.3 ppm as compared with the analogous signal of progenin (Table 1).

The values of the chemical shifts of the carbon atoms of the carbohydrate residues showed the pyranose form of all the monosaccharides, and also the β configuration of the glycosidic center of the D-glucose residue and the α configuration of the anomeric centers of the L-arabinose and L-rhamnose residues [6, 7].

The conclusion concerning the configurations of the glycosidic bonds was also confirmed by the PMR spectrum of cyclofoetoside B (I), in which doublets were observed of the anomeric protons of β-D-glucopyranose (4.70; ^3J =7.8 Hz), α-L-arabinopyranose (4.95; ^3J = 6.3 Hz), and L-rhamnose (5.48 ppm, ^3J = 1.4 Hz) [8].

Consequently, cyclofoetoside B is a bisdesmoside of cyclofoetigenin B the carbohydrate components of which, L-arabinose and rutinose, are present at C-3 and C-16, respectively.

Thus, cyclofoetoside B has the structure of 24S-cycloartane-3β,16β,24,25,30-pentaol 3-O-α-L-arabinopyranoside 16-O-[O-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside].

EXPERIMENTAL

For general remarks, see [1]. The following solvent systems were used: 1) chloroform–methanol (15:1); 2) benzene–ethyl acetate (3:1); and 3) chloroform–methanol–water (70:12:1).

PMR spectra were recorded on XL-200 (Varian) and JNM-4H-100/100 MHz instruments in deuteropyridine (δ, ppm, 0 is TMS or HMDS), and ^{13}C NMR spectra on a CFT-20 instrument (Varian) (δ, ppm, 0 is TMS).

For the isolation of cyclofoetoside B, see [1].

Cyclofoetoside B (I): $C_{47}H_{80}O_{18}$, mp 194-197°C, (from methanol); $[\alpha]_D^{24}$ +15.7 ± 2° (c 0.88; pyridine); ν_{max}^{KBr}, cm^{-1}: 3560-3200 (OH), 3035 (CH_2 of a cyclopropane ring). PMR (C_5D_5N, 0 is TMS): 0.24 and 0.45 (2 H-19, d, ^2J = 4.0 Hz); 0.97 (3 H, s, CH_3); 1.01 (3 H, d, ^3J = 7.7 Hz, CH_3-21); 1.24 (3 H, s, CH_3); 1.52 (9 H, (s, 3 × CH_3); 1.65 (3 H, d, ^3J = 6.1 Hz, CH_3– of a L-rhamnopyranosyl residue); 3.6-4.7 (m, H-3, H-16, H-24, and carbohydrate protons); 4.70 (1 H, d, ^3J = 7.8 Hz, anomeric proton of a D-glucopyranose residue); 4.95 (1 H, d, ^3J = 6.3 Hz, anomeric proton of a L-arabinopyranoside residue); and 5.48 (1 H, d, ^3J = 1.4 Hz, anomeric proton of a L-rhamnopyranose residue).

The methanolysis of glycoside (I) in anhydrous methanol containing 5% of HCl for 12 h followed by the analysis of the carbohydrates by GLC [3] showed the presence of D-glucose, L-arabinose, and L-rhamnose in a ratio of 1.00:1.28:1.36.

TABLE 1. Chemical Shifts of the Carbon Atoms in Compounds (I) and (III)-(V) (C_5D_5N, δ, ppm, 0 is TMS)

C atom		I	III	IV	V
1		32,2	32,4	32,4	32,5
2		30,0	30,7*	30,7*	30,8*
3		89,6	80,3	80,2	80,3
4		45,0	43,9	43,7	43,8
5		48,0	48,0	47,9	48,0
6		21,9	21,9	21,8	21,9
7		26,5*	26,9	26,5*	26,8*
8		48,6	48,5	48,3	48,5
9		21,3	21,3	21,1	21,7
10		26,2*	26,4	26,2*	26,2*
11		25,7*	26,5	26,2*	26,4*
12		33,6	33,4	33,4	33,6
13		45,8	45,8	45,8	45,8
14		47,0	47,1	47,0	47,0
15		48,1	48,8	48,3	48,5
16		82,7	72,1	82,6	82,7
17		57,8	57,5	57,7	57,9
18		17,5	18,2	17,5	17,5
19		30,0	31,7*	31,7	31,8
20		29,6	28,8	29,5*	29,5*
21		19,7	19,5	19,7	19,7
22		33,2	33,1	33,0	33,1
23		28,9	28,1	28,8*	28,8*
24		77,1	77,3	78,0	78,0
25		72,7	72,6	72,8	72,8
26		26,2*	26,5*	26,2*	26,7*
27		25,7	25,6	25,6	25,6
28		20,6	20,4	20,5	20,6
29		21,3	21,7	21,6	21,7
30		63,5	64,6	64,5	64,5
D-Glucose	C-1	106,5		105,6	106,6
	C-2	75,6		75 7	75,6
	C-3	78,4		78,4	78,4
	C-4	71,9		71,9	71,9
	C-5	76,7		78,0	76,7
	C-6	68,4		63,3	68,4
L-Rhamnose	C-1	102,2			102,3
	C-2	72,3			72,3
	C-3	72,7			72,8
	C-4	74,0			74,0
	C-5	69,5			69,7
	C-6	18,6			18,6
L-Arabinose	C-1	106,1			
	C-2	72,7			
	C-3	74,0			
	C-4	68,7			
	C-5	65,7			

*Assignment ambiguous within a column.

25-Norcycloartane-3β,16β,24,30-tetraol (II) from (I). With stirring, a solution of 1 g of sodium periodate in 10 ml of water was added to 500 mg of cyclofoetoside B (I) in 50 ml of methanol and the mixture was left at room temperature for 24 h. Then it was diluted with 50 ml of water, and 5 ml of glycerol was added. The methanol was distilled off and the remaining solution was extracted with chloroform. The residue after the evaporation of the chloroform was dissolved in 100 ml of methanol. To this solution, 1 g of sodium tetrahydroborate was added in small portions. After an hour, the reaction mixture was acidified with 5% sulfuric acid to pH 1 and was then left at room temperature for 24 h. After this, it was diluted with water, the methanol was evaporated off, and the remaining solution was extracted with chloroform. The residue after the evaporation of the chloroform was dissolved in 100 ml of methanol. To this solution, 1 g of sodium tetrahydroborate was added in small portions. After an hour, the reaction mixture was acidified with 5% sulfuric acid to pH 1 and was then left at room temperature for 24 h. After this, it was diluted with water, the methanol was evaporated off, and the remaining solution was extracted with chloroform. The residue after the working up of the chloroform extract and the evaporation of the solvent was chromatographed on a column with elution by system 1. This gave 100 mg of the nor- compound (II), $C_{27}H_{29}O_4$, mp 232-235°C (from methanol), $[\alpha]_D^{22}$ +80 ± 2° (c 0.6; methanol), ν_{max}^{KBr}, cm^{-1}; 3500-3260 (OH), 3035 (CH_2 of a cyclo-

propane ring). Mass spectrum, m/z (%): M^+ 434 (6.4), 416 (46.2), 401 (100), 398 (51.3), 383 (43.6), 375 (26.9), 367 (12.8), 365 (12.8), 357 (23.1), 332 (38.5), 313 (78.2), 311 (24.4), 297 (23.1), 277 (24.4), 263 (17.9). PMR (C_5D_5N, 0 is HMDS): 0.22 and 0.34 (2 H-19, d, ^2J = 4 Hz); 0.80 (3 H, s, CH_3); 0.93 (3 H, d, CH_3-21, ^3J = 6 Hz); 1.26 (3 H, s, CH_3); 1.37 (3 H, s, CH_3); 3.47 (H-3, m); 3.62 (H-30, d, ^2J = 11 Hz); 3.77 (2 H-24, t, ^3J = 7.5 Hz); 4.50 H-30, d, ^3J = 11 Hz; H-16, m).

25-Norcycloartane-3β,16β,24,30-tetraol 3β,16β,24,30-Tetraacetate (VI) from (II). Substance (II) (73 mg) was acetylated with 1 ml of acetic anhydride in 2 ml of pyridine at room temperatue for 36 h. The residue after the solvent had been distilled off was chromatographed on a column, with elution by system 2. This gave 100 mg of the tetraacetate (VI), $C_{38}H_{52}O_8$, mp 132-135°C (from chloroform–methanol (1:1)), $[\alpha]_D^{22}$ +76 ± 2° (c 1.0; methanol), ν_{max}^{KBr}, cm^{-1}; 3050 (CH_2 of a cyclopropane ring), 1740, 1245 (esters). Mass spectrum, m/z (%): M^+ 602 (1.3), 542 (35.5), 527 (56.6), 482 (100), 467 (52.0), 459 (11.8), 441 (7.9), 422 (21.1), 413 (67.1), 407 (52.6), 399 (11.8), 355 (35.5), 353 (23.7), 293 (56.6). PMR (C_5D_5N, 0 is HMDS): 0.24 and 0.44 (2 H-19, d, ^2J = 4 Hz); 0.74 (3 H, s, CH_3); 0.81 (3 H, d, CH_3-21); 0.96 (3 H, s, CH_3); 1.01 (3 H, s, CH_3); 1.91 (6 H, s, 2 × CH_3COO); 1.95 (3 H, s, CH_3COO); 1.99 (3 H, s, CH_3COO); 3.96 (2 H-24, t, ^3J = 7.5 Hz); 4.42 (2 H-30, AB quartet, ^2J = 12.5 Hz); 4.66 (H-3, m); 5.27 H-16, m).

Enzymatic Hydrolysis of Cyclofoetoside B. To 500 mg of glycoside (I) in 0.5 liter of water was added 10 ml of ethanol and 5 ml of the gastric juice of the grape snail. The solution was left at +38°C for 20 days, after which the hydrolysate was treated with butanol. The evaporated butanolic extract was chromatographed on a column with elution by system 1. This gave 14 mg of substance (III) with mp 239-241°C (methanol), $[\alpha]_D^{22}$ +72 ± 2° (c 0.5; methanol), which was shown to be identical with cyclofoetigenin B [2] also by the characteristics of its IR, mass, and PMR spectra.

Further elution of the column with system 3 led to the isolation of progenins (IV) (116 mg) and (V) (89 mg).

Cyclofoetigenin B 16-O-β-D-glucopyranoside (IV) from (I). Glucoside (IV), $C_{36}H_{62}O_{10}$, mp 223-225°C (from acetone), $[\alpha]_D^{24}$ +37 ± 2° (c 0.97; methanol). It was shown with the aid of GLC [3] that progenin (IV) contained one D-glucose residue. ν_{max}^{KBr}, cm^{-1}; 3500-3200 (OH); 3035 (CH_2 of a cyclopropane ring). PMR (C_5D_5N, 0 is TMS): 0.31 and 0.36 (2 H-19, d, ^2J = 4.0 Hz); 0.88 (3 H, s, CH_3); 1.05 (3 H, d, ^3J = 6 Hz, CH_3-21); 1.27 (3 H, s, CH_3); 1.53 (9 H, s, 3 × CH_3); 4.76 (1 H, d, ^3J = 7.5 Hz, anomeric proton of a D-glucopyranose residue).

Cyclofoetigenin B 16-O-[O-α-L-Rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside) (V) from (I). Progenin (V), $C_{42}H_{72}O_{14}$, mp 229-231°C (from methanol), $[\alpha]_D^{30}$ +41 ± 2° (c 0.7; methanol). According to GLC, glycoside (V) contained one residue each of D-glucose and L-rhamnose. ν_{max}^{KBr}, cm^{-1}: 3530-3280 (OH); 3035 (CH_2 of a cyclopropane ring). PMR (C_5D_5N, 0 is TMS): 0.31 and 0.44 (2 H-19, d, ^2J = 4.0 Hz); 0.98 (3 H, s, CH); 1.02 (3 H, d, ^3J = 6.3 Hz, CH_3-21); 1.26 (3 H, s, CH_3); 1.49 (3 H, s, CH_3); 1.53 (6 H, s, 2 × CH_3); 1.65 (3 H, d, ^3J = 6.0 Hz, CH_3 of a L-rhamnopyranosyl residue); 4.72 (1 H, d, ^3J = 7.5 Hz, anomeric proton of a D-glucopyranose residue); 5.49 (1 H, d, ^3J = 1.0 Hz, anomeric proton of a L-rhamnopyranosyl residue).

SUMMARY

A new glycoside of the cycloartane series — cyclofoetoside B — has been isolated from the epigeal part of the plant *Thalictrum foetidum* L. (Ranunculaceae); it has the structure of 24S-cycloartane-3β,16β,24,25,30-pentaol 3-O-α-L-arabinopyranoside 16-L-[O-α-L-rhamnopyranosyl-(1 → 6)-β-D-glucopyranoside].

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CIRCULAR DICHROISM OF THE ALKALOIDS OF *Petilium raddeanum*

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The circular dichroism (CD) method has been used for studying the stereochemistry of steroid alkaloids containing an azomethine ring — petiline and petisine. In the CD spectrum of petiline a Cotton effect (CE) is observed in the 235 nm region which is due to a $n \rightarrow \pi^*$ transition in the azomethine chromophore. The negative sign of this CE shows the 25S configuration in petiline. An analysis of CD spectra has shown that the 25S configuration is retained when petiline is oxidized to petisine.

In order to determine the absolute configuration of the asymmetric center at C_{25} in the steroid alkaloids containing an azomethine ring, petiline (I) and petisine (II) [1, 2], we have considered their circular dichroism (CD) spectra and also, the CD spectra of 0,0^1—diacetyl-23-pseudosolasodine (III), and 0,0'-diacetyl-23-oxopseudosolasodine (IV) [3]. In their CD spectra, cyclic azomethines have a Cotton effect (CE) in the 230-250 nm region which is due to a $n \rightarrow \pi^*$ transition in the C=N chromophore, the sign of which has enabled the conformation of the ring and the configuration of the asymmetric center at C_{25} to be determined.

Figure 1 shows the two chiral conformations of the azomethine ring with the 25R (a) and 25S (b) configurations, which exhibit positive and negative Cotton effects, respectively, in the CD spectra.

It can be seen from the figures given in Table 1 that there is a negative CE in the 240 nm region of the CD spectrum of petiline and, consequently, petiline can be assigned to the 25S series. In addition to petiline, the alkaloid petisine was isolated from *Petilium raddeanum*, and this, as has been established, is the 23-oxo derivative of petiline [2].

In the CD spectrum of petisine, the azomethine CE is shifted into the 280-290 nm region thanks to the conjugation of the azomethine with the carbonyl group. In petiline and petisine there is another carbonyl group, at C_6, which also absorbs in the 290 nm region. Consequently, in the CD spectrum of petisine, a broad intense CE is observed in the 280-300 nm region with an inflection at 291 nm. Petisine can be obtained by the oxidation of petiline with manganese dioxide [2]. In order to exclude the influence of a second carbonyl group in the CD spectrum, the oxidation of the known alkaloid 0,0'-diacetylpseudosolasodine, which does not contain a carbonyl group at C_6, was performed under the same conditions. The negative CE in the CD spectrum of the resulting 0,0'-diacetyl-23-oxopseudosolasodine observed in the 270-290 nm region can be assigned unambiguously to the absorption of the conjugated chromophore O=C—C=N.

It can be seen from Dreiding models that in the least strained conformation of the azomethine ring in compounds (II) and (IV) the azomethine bond and the carbonyl group are located in the same plane (Fig. 1c). Such types of arrangement have been reported previously for monocyclic α,β-unsaturated ketones [5]. With such an arrangement, the carbonyl group does not change the intrinsic conformation of the azomethine ring. It can be seen from the octant diagram for the azomethine ring (Fig. 1d) that the contribution to the rotational force of the $n \rightarrow \pi^*$ transition due to the chirality of the O=C—C=N chromophore is zero, since it has a planar arrangement and the value and sign of the CE are determined by the conformation of the ring and of the methyl group at C_{25}.

Thus, the negative CE in the CD spectra of compounds (II) and (IV) permits them to be assigned to the 25S series.

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