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TRITERPENE GLYCOSIDES FROM *Astragalus* AND THEIR GENINS. XCI. CHEMICAL TRANSFORMATION OF CYCLOARTANES. X. SYNTHESES BASED ON CYCLOALPIOSIDE D AND CYCLOALPIGENIN D

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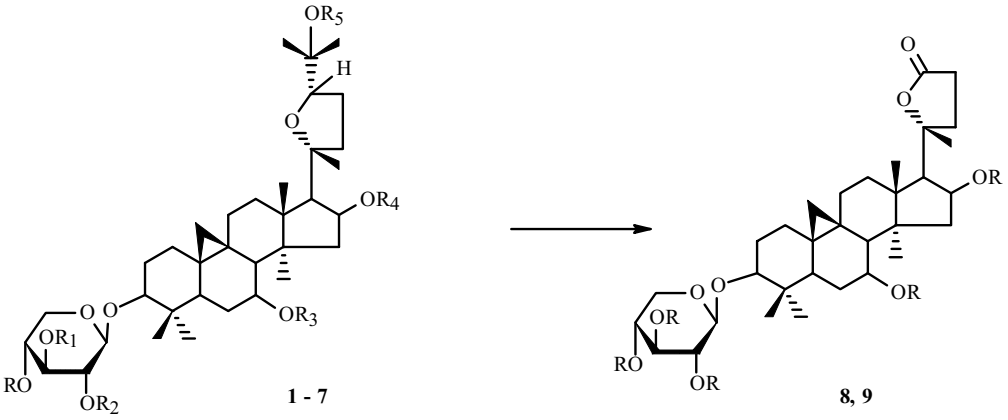
Nine new compounds that may be of interest as potential biologically active compounds and as materials for further chemical transformation were synthesized from the principal glycoside of Astragalus alopecurus *Pall. (Leguminosae) cycloalpioside D and its genin cycloalpigenin D.*

Keywords: *Astragalus*, Leguminosae, cycloartanes, cycloalpigenin D, cycloalpioside D, PMR, ^{13}C NMR, DEPT spectra.

Triterpene glycosides of the cycloartane series that contain β-D-xylopyranose acetylated to various extents on C-3 of the genin are known to exhibit several biological activities. Examples of these are cyclosiversioside D, the monoacetyl derivative of cyclosiversioside F, and several other derivatives of cyclosiversioside F. Antiviral and antitumor activity and low toxicity have been reported for these compounds. They are also known to be interferon inductors [1, 2].



1: R = R_1 = R_2 = R_3 = R_4 = R_5 = H; **2:** R = R_1 = R_2 = R_3 = Ac, R_4 = R_5 = H
3: R = R_1 = R_2 = Ac, R_3 = R_4 = R_5 = H; **4:** R = R_1 = Ac, R_2 = R_3 = R_4 = R_5 = H
5: R = R_2 = R_3 = R_4 = R_5 = H, R_1 = Ac; **6:** R = R_1 = R_2 = R_3 = R_4 = R_5 = Ac
7: R = R_1 = R_2 = R_3 = R_4 = Ac, R_5 = H

8: R = Ac
9: R = H

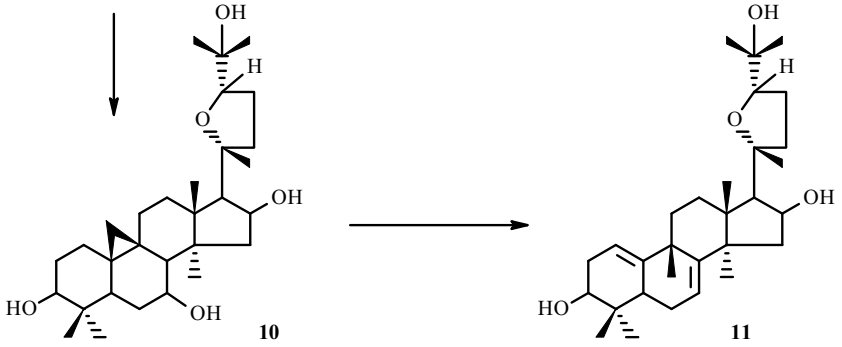


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TABLE 1. Chemical Shifts of C Atoms in **1**–**7** (100 MHz, C_5D_5N, δ, ppm, 0 = TMS)

C atom	DEPT	**1**	**2**	**3**	**4**	**5**	**6**	**7**
1	CH_2	31.84*	31.26	31.71	31.66	31.72[a]	31.80	31.36
2	CH_2	29.93	29.30	29.43	29.64	29.76	29.83[a]	29.34
3	CH	88.23	88.43	88.78	88.47	88.45	88.77	88.32
4	C	41.03	40.58	40.58	40.86	40.91	41.03	40.57
5	CH	46.37[a]	45.28	46.13	46.20	46.28	45.80	45.36
6	CH_2	31.75*	27.35	31.51	31.62	31.72[a]	27.32	27.41
7	CH	70.23	72.36	70.19	70.15	70.19	73.08	72.29
8	CH	55.10	51.21	55.09	54.94	54.98	52.09	51.65
9	C	20.04	19.63	20.08	20.00	20.04	19.84	19.37
10	C	27.08	26.88	26.90	26.93	27.04	27.71	26.84[a]
11	CH_2	26.45	26.43	26.40	26.36	26.37	26.78[b]	26.30
12	CH_2	33.40	33.05	33.37	33.33	33.38	32.66	32.25
13	C	45.52	45.54	45.54	45.48	45.53	46.65	46.15
14	C	46.37[a]	45.89	46.34	46.31	46.34	47.51	46.87
15	CH_2	48.78	48.09	48.78	48.62	48.68	48.11	47.63
16	CH	73.77	73.45	73.75	73.72	73.73	76.72	76.31
17	CH	57.98	57.85	57.99	57.93	57.96	57.69	57.16
18	CH_3	21.25	21.18	21.25	21.16	21.18	21.20	21.57
19	CH_2	28.86	28.66	28.78	28.73	28.78	29.83[a]	29.40
20	C	87.31	87.16	87.30	87.27	87.28	86.29	85.63
21	CH_3	28.64	28.56	28.60	28.56	28.56	27.86	26.84[a]
22	CH_2	35.02	35.09	35.05	34.99	35.04	37.90	37.13
23	CH_2	26.75	26.49	26.69	26.69	26.73	26.78[b]	26.61
24	CH	81.70	81.84	81.76	81.70	81.74	81.91	83.05
25	C	71.21[b]	71.30	71.22	71.21	71.21	83.47	70.82
26	CH_3	27.12	27.12	27.08	27.02	27.04	22.84	25.01
27	CH_3	28.22	28.13	28.14	28.10	28.11	22.30	27.71
28	CH_3	19.87	20.00	19.85	19.81	19.84	20.59	20.14
29	CH_3	25.73	25.11	25.32	25.52	25.62	25.46	26.56
30	CH_3	15.30	14.87	14.95	15.10	15.17	15.34	14.88
				β-D-Xyl*p*				
1	CH	107.51	103.27	103.26	106.65	106.98	103.76	103.30
2	CH	75.51	72.72	72.29	72.68	73.00	72.74	72.62
3	CH	78.55	73.40	72.65	75.53	79.19	73.76	73.30
4	CH	71.21[b]	69.84	69.79	70.50	69.15	70.22	69.77
5	CH_2	67.11	62.84	62.47	62.70	66.66	62.95	62.51
				Ac				
COO	C	–	170.18	170.23	170.47	170.78	170.68	170.30
			170.18	170.01	170.27		170.68	170.21
			170.00	169.55			170.57	170.12
			169.55				170.47	170.02
							170.03	169.58
							168.65	
CH_3	CH_3	–	21.61	20.66	20.80	21.12	22.08	21.62
			20.66	20.51	20.58		21.97	20.89
			20.52	20.48			21.20[c]	20.67
			20.49				21.20[c]	20.52[b]
							20.97	20.52[b]
							20.97	

Resonances marked with the same letters overlap each other within a column; with an asterisk, are assigned ambiguously.

Therefore, it became obvious that the preparation of similar derivatives of other representative cycloartane glycosides is highly interesting with respect to the search for new biologically active compounds.

We performed the present investigation using cycloalpioside D (**1**) as the starting material. This is the principal glycoside contained in *Astragalus alopecurus* Pall. (Leguminosae). It has the structure cycloalpigenin D 3-*O*-*β*-D-xylopyranoside.

In the first step, cycloalpioside D was acetylated by acetic anhydride in Py for 1.5 h at ~13°C. This produced four products (**2**–**5**) that were separated by column chromatography.

The PMR spectrum of **2** showed resonances for four acetyls at δ 1.85, 1.89, 1.90, and 1.99. This indicated that this product was a tetraacetate. Resonances of H-2, H-3, and H-4 of the *β*-D-xylopyranose and H-7 in the same spectrum underwent weak-field shifts compared with those of cycloalpioside D and were observed at δ 5.28, 5.55, 5.17, and 4.85, respectively. This defined **2** as cycloalpioside D 2′,3′,4′,7-tetraacetate. This was also confirmed by the ^{13}C NMR spectrum of **2** (Table 1).

The PMR spectrum of **3** exhibited resonances for three acetyls at δ 1.85, 1.91, and 2.00, indicating that this product was cycloalpioside D triacetate. Because the resonances of *β*-D-xylopyranose H-2, H-3, and H-4 were located at weak field of δ 5.31, 5.57, and 5.19, all acetyls were located on the carbohydrate part of the molecule. This meant that **3** was cycloalpioside D 2′,3′,4′-triacetate. This conclusion agreed completely with ^{13}C NMR spectral data of **3** (Table 1).

Resonances for two acetyls appeared at δ 1.87 and 1.90 in the PMR spectrum of **4**. This indicated that this product was a diacetate. The locations of the acetyls in **4** were inferred from the same PMR spectrum where the resonances of *β*-D-xylopyranose H-3 and H-4 were shifted to weak field and observed at δ 5.60 and 5.18, respectively. Therefore, **4** was cycloalpioside D 3′,4′-diacetate. The ^{13}C NMR spectral data for **4** were consistent with this structure.

A resonance for one acetyl was found at δ 1.87 in the PMR spectrum of **5**. This indicated that this compound was a monoacetate. A weak-field shift of the resonance for H-3 of *β*-D-xylopyranose to δ 5.59 provided evidence that the acetyl was located on C-3 of the monosaccharide and that **5** was cycloalpioside D 3′-monoacetate. As expected, the resonance for C-3 of *β*-D-xylopyranose in the ^{13}C NMR spectrum of **5** was shifted to weak field compared with that in the spectrum of cycloalpioside D and was found at δ 79.19 (Table 1).

The reaction was carried out at 16°C for 16 d in order to prepare pentaacetate **7**, the key product for further transformations, as the predominant product. As a result, the required **7** in addition to two side products **2** and **6** was obtained as the major product. The structures of these compounds were also confirmed using NMR spectroscopy.

Resonances of six acetyls were observed in the PMR spectrum of **6** at δ 1.84, 1.89, 1.908, 1.914, 1.99, and 2.00. Therefore **6** was cycloalpioside D peracetate. The ^{13}C NMR spectrum of **6**, where resonances of six acetyls were noted, led to this same conclusion (Table 1).

The PMR spectrum of **7** exhibited resonances of five acetyls at δ 1.85, 1.90, 1.91, 1.99, and 2.00. Resonances of five protons geminal to the acetyls underwent weak-field shifts. This meant that **7** was acetylated at all secondary hydroxyls and only the tertiary hydroxyl on C-25 of the side chain remained free. In fact, the resonance of C-25 in the ^{13}C NMR spectrum of **7** did not experience significant changes and was observed at δ 70.82. These data defined **7** as cycloalpioside D 2′,3′,4′,7,16-pentaacetate.

In this instance, insignificant amounts of peracetate **6** and tetraacetate **2** were obtained as undesired products. If tetraacetate **2** was avoided by prolonging the reaction time, then the amount of peracetate **6** increased slightly. Peracetate **6** in this synthesis was responsible for the principal losses of starting compound.

Another direction for the chemical transformation of cycloalpioside D was the preparation of cycloalpioside D lactone (**9**). The interest in such a compound was predicated on the fact that preparation of the analogous lactone from cyclosiversioside F enhanced substantially the cardiotonic activity of the starting compound [3].

Pentaacetate **7** was oxidized by Jones reagent in order to introduce the lactone into the side chain [4]. This produced the pentaacetate of the lactone **8**. The IR spectrum, in which an absorption band at 1760 cm^{-1} was noted, indicated that the *γ*-lactone ring was introduced. This conclusion was confirmed by the PMR and ^{13}C NMR spectra. The PMR spectrum of **8** showed resonances of five methyls at strong field. This indicated that the hydroxyisopropyl moiety was missing in the side chain. As expected, the H-24 resonance was missing in the same spectrum. The chemical shifts of C-20 (δ 89.33) and C-24 (δ 176.79) in the ^{13}C NMR spectrum of **8** (Table 2) were consistent with the introduction of a lactone ring. Basic hydrolysis of **8** with subsequent acidification formed desired product **9**, the structure of which was confirmed analogously.

The IR spectrum of **9** contained an absorption band at 1756 cm^{-1} that was characteristic of a *γ*-lactone ring. Resonances of five methyls were observed at strong field in the PMR spectrum of **9**. This indicated that the hydroxyisopropyl moiety was missing in the side chain. Resonances of acetyls were missing in the same spectrum, suggesting that all protecting groups were removed. The chemical shifts of C-20 (δ 90.41) and C-24 (δ 177.28) in the ^{13}C NMR spectrum of **9** also were consistent with retention of the *γ*-lactone ring (Table 2). These data defined **9** as 3-*O*-*β*-D-xylopyranoside-20*R*-25-norcycloartan-3*β*,7*β*,16*β*-triol-20,24-olide.

TABLE 2. Chemical Shifts of C Atoms in **8**–**11** (100 MHz, C_5D_5N, δ, ppm, 0 = TMS)

C atom	DEPT	**8**	**9**	**10**	**11**
1	CH_2	32.64	31.89[a]	32.21	119.61
2	CH_2	31.83	29.23	31.15	31.35*
3	CH	88.76	88.21	77.77	73.38
4	C	41.04	41.03	40.82	40.16
5	CH	45.80	46.47[b]	46.31	42.23
6	CH_2	27.84	31.89[a]	32.09	31.03*
7	CH	73.10	70.23	70.38	115.22
8	CH	51.78	55.07	55.30	142.32
9	C	19.62	19.78	19.98	37.18
10	C	27.30	27.09	27.39	139.74
11	CH_2	26.40	26.48	26.46	25.19
12	CH_2	33.53	33.14	33.44	33.45
13	C	46.60	46.22	45.57	46.90
14	C	47.06	46.47[b]	46.39	47.78
15	CH_2	47.13	50.78	48.95	45.36
16	CH	76.26	72.32	73.80	72.68
17	CH	56.45	57.50	58.01	56.84
18	CH_3	21.58	21.45	21.38	20.02
19	CH_2	29.60	29.93[c]	29.23	32.24
20	C	89.33	90.41	87.32	87.19
21	CH_3	29.56	30.28	28.67	28.64
22	CH_2	29.79	29.93[c]	35.05	34.82
23	CH_2	32.95	32.84	26.77	26.52
24	CH	176.79	177.28	81.73	81.62
25	C	–	–	71.22	71.42
26	CH_3	–	–	27.14	27.04
27	CH_3	–	–	28.22	28.08
28	CH_3	20.11	19.78	19.92	18.11
29	CH_3	25.49	25.75	26.20	23.85
30	CH_3	15.36	15.31	14.74	19.22
		β-D-Xyl*p*			
1	CH	103.76	107.53		
2	CH	72.77	75.53		
3	CH	73.63	78.60		
4	CH	70.24	71.21		
5	CH_2	62.98	67.11		
		Ac			
COO	C	170.67	–		
		170.55			
		170.47			
		170.21			
		170.04			
CH_3	CH_3	22.07	–		
		21.45			
		21.13			
		21.00			
		20.98			

Resonances marked with the same letters overlap each other within a column; with an asterisk, are assigned ambiguously.

The next transformation in our research was distinguished by the fact that a structural fragment of cycloartane triterpenoids, the cyclopropane ring, was involved in the transformation. The subject of the study was cycloalpigenin D (**10**), which is the genin of cycloalpioside D. Reaction of **10** and benzenesulfonylchloride in Py formed di-unsaturated triterpenoid

11. The observation of resonances for eight methyls in the PMR spectrum of the latter indicated that the cyclopropane ring was opened in this compound [5]. Resonances for four olefinic C atoms were found in the ^{13}C NMR spectrum of **11**. Their chemical shifts indicated that the olefins were trisubstituted. This was also indicated in the PMR spectrum where a 2H resonance for the olefinic protons was noted at δ 5.46. Because a resonance for a proton geminal to the 7*β*-hydroxyl was missing in this spectrum, one of the double bonds was situated at C-7–C-8 and arose as a result of dehydration of the 7*β*-hydroxyl.

The second double bond arose as a result of opening of the three-membered ring and could have alternate C-1–C-10 or C-9–C-11 positions depending on which C–C bond was opened. The location of the second double bond was elucidated as follows. As already noted, the olefinic protons resonated as a 2H doublet of doublets at δ 5.46. Resonances for two pairs of methylene protons were observed in a difference PMR spectrum upon pre-irradiation of this resonance. Obviously one pair of resonances belonged to the C-6 protons.

The other pair of resonances was also assigned as the result of a double resonance experiment. Pre-irradiation of the H-3 resonance at δ 3.67 produced in a difference PMR spectrum a single pair of aforementioned resonances (δ 2.54 and 2.28) that indicated unambiguously that these resonances belonged to the C-2 methylene protons. Therefore, the other olefinic bond was situated at C-1–C-10. This meant that the C-10–C-19 bond had opened and formed *abeo*-lanostadiene **11** with the structure 20*R*,24*S*-epoxy-19(10→9)-*abeo*-lanosta-1(10),7-diene-3*β*,16*β*,25-triol.

Thus, a series of semi-synthetic triterpenoids was prepared starting from cycloalpioside D and cycloalpigenin D. The compounds are of independent interest as biologically active compounds and as materials for further transformation.

EXPERIMENTAL

General comments were published [6]. We used the solvent systems $CHCl_3$:MeOH (25:1, 1; 10:1, 2; 30:1, 3; 45:1, 4) and $CHCl_3$:MeOH:H_2O (70:12:1, 5). PMR spectra were recorded from Py-d_5 solutions (δ, ppm, 0 = HMDS) on a UNITYplus 400 spectrometer (Varian); ^{13}C NMR spectra, on the same spectrometer with full C–H decoupling and also under DEPT conditions. Chemical shifts of C atoms were referenced to the resonance of the *β*-C atoms of Py-d_5 (δ 123.493 vs. TMS).

Cycloalpioside D (1) was the starting compound and was isolated from the aerial part of *A. alopecurus* Pall. (Leguminosae) as before [7], $C_{35}H_{58}O_9$, mp 300–301°C (MeOH).

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.13 and 0.64 (d, $^2J = 4$, 2H-19), 0.93, 0.99, 1.17, 1.21, 1.22, 1.39, 1.45 (s, 7 × CH_3), 1.91 (d, $^3J = 9$, H-8), 2.40 (d, $^3J = 7.8$, H-17), 2.65 (dd, $^2J = 13.6$, $^3J = 8$, H-15), 3.00 (td, $^2J = {}^3J_1 = 11.3$, $^3J_2 = 9$, H-22), 3.38 (dd, $^3J_1 = 11.8$, $^3J_2 = 4.2$, H-3), 3.64 (dd, $^2J = 11.3$, $^3J = 10$, *β*-D-xylopyranose H-5*a*), 3.67 (m, H-7), 3.76 (dd, $^3J_1 = 8.9$, $^3J_2 = 5.3$, H-24), 3.90 (dd, $^3J_1 = 8.7$, $^3J_2 = 7.6$, *β*-D-xylopyranose H-2), 4.04 (t, $^3J_1 = {}^3J_2 = 8.7$, *β*-D-xylopyranose H-3), 4.11 (td, $^3J_1 = {}^3J_2 = 10$, $^3J_3 = 5.3$, *β*-D-xylopyranose H-4), 4.26 (dd, $^2J = 11$, $^3J = 5$, *β*-D-xylopyranose H-5*e*), 4.73 (d, $^3J = 7.6$, *β*-D-xylopyranose H-1), 4.96 (q, $^3J_1 = {}^3J_2 = {}^3J_3 = 7.8$, H-16).

Table 1 lists the ^{13}C NMR spectrum.

Cycloalpigenin D (10) was also used as a starting compound and was obtained via acid hydrolysis from cycloalpioside D as before [7], $C_{30}H_{50}O_5$, mp 209–211°C (MeOH).

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.20 and 0.69 (d, $^2J = 4$, 2H-19), 0.98, 1.02, 1.10, 1.17, 1.23, 1.42, 1.46 (s, 7 × CH_3), 1.93 (d, $^3J = 8.8$, H-8), 2.41 (d, $^3J = 7.9$, H-17), 2.68 (dd, $^2J = 13.7$, $^3J = 8$, H-15), 3.02 (td, $^2J = {}^3J_1 = 11.6$, $^3J_2 = 8.8$, H-22), 3.42 (dd, $^3J_1 = 11.6$, $^3J_2 = 4.4$, H-3), 3.69 (td, $^3J_1 = {}^3J_2 = 10$, $^3J_3 = 4$, H-7), 3.78 (dd, $^3J_1 = 8.8$, $^3J_2 = 5.3$, H-24), 4.98 (q, $^3J_1 = {}^3J_2 = {}^3J_3 = 7.4$, H-16).

Table 2 lists the ^{13}C NMR spectrum.

2′,3′,4′,7-Tetraacetate (2), 2′,3′,4′-Triacetate (3), 3′,4′-Diacetate (4), and 3′-Monoacetate (5) of Cycloalpioside D from 1. Cycloalpioside D (**1**, 1 g) was acetylated by acetic anhydride (5 mL) in anhydrous Py (15 mL) for 1.5 h at 13°C and poured onto ice. The resulting precipitate was filtered off, washed with H_2O, and dried. The dry solid was chromatographed over a column of silica gel with elution by system 1 to isolate **2** (384 mg), $C_{43}H_{66}O_{13}$, which partially melted at 143–145°C, solidified, and melted again at 200–213°C (MeOH).

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.15 and 0.56 (d, $^2J = 4.6$, 2H-19), 0.77, 0.83, 0.834, 1.18, 1.20, 1.34, 1.46 (s, 7 × CH_3), 1.85, 1.89, 1.90, 1.99 (s, 4 × Ac), 2.31 (d, $^3J = 7.7$, H-17), 2.97 (td, $^2J = {}^3J_1 = 11$, $^3J_2 = 9$, H-22), 3.16 (dd, $^3J_1 = 11.7$, $^3J_2 = 4.4$, H-3), 3.54 (dd, $^2J = 11.6$, $^3J = 9.7$, *β*-D-xylopyranose H-5*a*), 3.77 (dd, $^3J_1 = 9$, $^3J_2 = 5.4$, H-24), 4.17 (dd, $^2J = 11.6$, $^3J = 5.4$, *β*-D-xylopyranose H-5*e*), 4.74 (d, $^3J = 7.4$, *β*-D-xylopyranose H-1), 4.85 (m, H-7, H-16),

5.17 (td, $^3J_1 = {}^3J_2 = 9.7$, $^3J_3 = 5.4$, β-D-xylopyranose H-4), 5.28 (dd, $^3J_1 = 9.5$, $^3J_2 = 7.5$, β-D-xylopyranose H-2), 5.55 (t, $^3J_1 = {}^3J_2 = 9.2$, β-D-xylopyranose H-3).

Table 1 lists the ^{13}C NMR spectrum.

Continued elution of the column by the same solvent system isolated **3** (170 mg), $C_{41}H_{64}O_{12}$, which partially melted at 140–145°C, solidified, partially melted again at 197–200°C, solidified, and melted finally at 226–228°C (MeOH).

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.11 and 0.59 (d, $^2J = 4$, 2H-19), 0.80, 0.91, 0.98, 1.18, 1.23, 1.39, 1.46 (s, 7 × CH_3), 1.85, 1.91, 2.00 (s, 3 × Ac), 1.89 (d, $^3J = 9$, H-8), 2.40 (d, $^3J = 7.8$, H-17), 2.65 (dd, $^2J = 13.6$, $^3J = 8$, H-15), 3.00 (q, $^2J = {}^3J_1 = {}^3J_2 = 11$, H-22), 3.20 (dd, $^3J_1 = 11.6$, $^3J_2 = 4.5$, H-3), 3.55 (dd, $^2J = 11.6$, $^3J = 9.8$, β-D-xylopyranose H-5*a*), 3.65 (td, $^3J_1 = {}^3J_2 = 10$, $^3J_3 = 4$, H-7), 3.77 (dd, $^3J_1 = 8.9$, $^3J_2 = 5.6$, H-24), 4.19 (dd, $^2J = 11.4$, $^3J = 5.4$, β-D-xylopyranose H-5*e*), 4.76 (d, $^3J = 7.4$, β-D-xylopyranose H-1), 4.95 (water resonance overlapped H-16 resonance), 5.19 (td, $^3J_1 = {}^3J_2 = 9.6$, $^3J_3 = 5.4$, β-D-xylopyranose H-4), 5.31 (dd, $^3J_1 = 9.4$, $^3J_2 = 7.4$, β-D-xylopyranose H-2), 5.57 (t, $^3J_1 = {}^3J_2 = 9.4$, β-D-xylopyranose H-3).

Table 1 lists the ^{13}C NMR spectrum.

Further elution of the column by the same solvent system isolated **4** (200 mg), $C_{39}H_{62}O_{11}$, which recrystallized at 203–205°C, melted at 223–226°C, solidified, and melted at 235–237°C (MeOH).

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.13 and 0.62 (d, $^2J = 4.2$, 2H-19), 0.86, 0.98, 1.13, 1.18, 1.23, 1.38, 1.46 (s, 7 × CH_3), 1.87, 1.90 (s, 2 × Ac), 2.40 (d, $^3J = 7.8$, H-17), 2.64 (dd, $^2J = 13.7$, $^3J = 8$, H-15), 2.98 (td, $^2J = {}^3J_1 = 11.2$, $^3J_2 = 9.2$, H-22), 3.32 (dd, $^3J_1 = 11.7$, $^3J_2 = 4.3$, H-3), 3.53 (dd, $^2J = 11.6$, $^3J = 9.8$, β-D-xylopyranose H-5*a*), 3.66 (td, $^3J_1 = {}^3J_2 = 9.9$, $^3J_3 = 4$, H-7), 3.77 (dd, $^3J_1 = 9$, $^3J_2 = 5.5$, H-24), 3.93 (dd, $^3J_1 = 9$, $^3J_2 = 7.4$, β-D-xylopyranose H-2), 4.19 (dd, $^2J = 11.4$, $^3J = 5.5$, β-D-xylopyranose H-5*e*), 4.75 (d, $^3J = 7.4$, β-D-xylopyranose H-1), 4.96 (td, $^3J_1 = {}^3J_2 = 7.8$, $^3J_3 = 6.7$, H-16), 5.18 (td, $^3J_1 = {}^3J_2 = 9.7$, $^3J_3 = 5{,}5$, β-D-xylopyranose H-4), 5.60 (t, $^3J_1 = {}^3J_2 = 9.3$, β-D-xylopyranose H-3).

Table lists the ^{13}C NMR spectrum.

Further elution of the column by solvent system 2 isolated **5** (50 mg), $C_{37}H_{60}O_{10}$, which recrystallized at 180–190°C and melted at 210–220°C (MeOH).

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.13 and 0.64 (d, $^2J = 4$, 2H-19), 0.88, 0.98, 1.14, 1.17, 1.22, 1.38, 1.45 (s, 7 × CH_3), 1.87 (s, Ac), 1.91 (d, $^3J = 9$, H-8), 2.39 (d, $^3J = 7.8$, H-17), 2.63 (dd, $^2J = 13.7$, $^3J = 8$, H-15), 2.98 (td, $^2J = {}^3J_1 = 11.3$, $^3J_2 = 9.6$, H-22), 3.33 (dd, $^3J_1 = 11.7$, $^3J_2 = 4.3$, H-3), 3.62 (dd, $^2J = 11.3$, $^3J = 10$, β-D-xylopyranose H-5*a*), 3.66 (td, $^3J_1 = {}^3J_2 = 9$, $^3J_3 = 4$, H-7), 3.77 (dd, $^3J_1 = 8.9$, $^3J_2 = 5.5$, H-24), 3.91 (dd, $^3J_1 = 9.5$, $^3J_2 = 7.6$, β-D-xylopyranose H-2), 4.10 (td, $^3J_1 = {}^3J_2 = 10$, $^3J_3 = 5.4$, β-D-xylopyranose H-4), 4.23 (dd, $^2J = 11.3$, $^3J = 5.4$, β-D-xylopyranose H-5*e*), 4.71 (d, $^3J = 7.5$, β-D-xylopyranose H-1), 4.95 (td, $^3J_1 = {}^3J_2 = 7.8$, $^3J_3 = 6.4$, H-16), 5.59 (t, $^3J_1 = {}^3J_2 = 9.2$, β-D-xylopyranose H-3).

Table 1 lists the ^{13}C NMR spectrum.

2′3′,4′,7,16,25-Hexaacetate (6), 2′,3′,4′,7,16-Pentaacetate (7), and 2′,3′,4′,7-Tetraacetate (2) of Cycloalpioside D from 1. Cycloalpioside D (**1**, 1 g) in dry Py (10 mL) was treated with acetic anhydride (5 mL), left at 16°C for 16 d, and poured onto ice. The resulting precipitate was filtered off, washed with H_2O, and dried. The solid was chromatographed over a column with elution by system 3 to isolate amorphous peracetate **6** (30 mg), $C_{47}H_{70}O_{15}$.

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.19 and 0.56 (d, $^2J = 4.5$, 2H-19), 0.79, 0.80, 0.83, 1.30, 1.33, 1.49, 1.49 (s, 7 × CH_3), 1.84, 1.89, 1.908, 1.914, 1.99, 2.00 (s, 6 × Ac), 2.33 (d, $^3J = 7.7$, H-17), 3.16 (dd, $^3J_1 = 11.5$, $^3J_2 = 4$, H-3), 3.55 (dd, $^2J = 11.7$, $^3J = 9.8$, β-D-xylopyranose H-5*a*), 4.06 (t, $^3J_1 = {}^3J_2 = 7.5$, H-24), 4.19 (dd, $^2J = 11.5$, $^3J = 5.4$, β-D-xylopyranose H-5*e*), 4.75 (d, $^3J = 7.5$, β-D-xylopyranose H-1), 4.81 (td, $^3J_1 = {}^3J_2 = 10.8$, $^3J_3 = 3.5$, H-7), 5.20 (td, $^3J_1 = {}^3J_2 = 9.9$, $^3J_3 = 5.4$, β-D-xylopyranose H-4), 5.32 (dd, $^3J_1 = 9.4$, $^3J_2 = 7.5$, β-D-xylopyranose H-2), 5.44 (td, $^3J_1 = {}^3J_2 = 8$, $^3J_3 = 4.7$, H-16), 5.60 (t, $^3J_1 = {}^3J_2 = 9.1$, β-D-xylopyranose H-3).

Table 1 lists the ^{13}C NMR spectrum.

Continued elution of the column by the same solvent system isolated a fraction containing a mixture of **6** and **7** (150 mg). The mixture contained a trace quantity of **6**.

Further elution of the column by the same solvent system gave **7** (335 mg), $C_{45}H_{68}O_{14}$.

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.19 and 0.56 (d, $^2J = 4.4$, 2H-19), 0.78, 0.79, 0.83, 1.25, 1.29, 1.30, 1.31 (s, 7 × CH_3), 1.85, 1.90, 1.91, 1.99, 2.00 (s, 5 × Ac), 2.39 (d, $^3J = 8$, H-17), 3.16 (dd, $^3J_1 = 11.6$, $^3J_2 = 4.4$, H-3), 3.54 (dd, $^2J = 11.6$, $^3J = 10$, β-D-xylopyranose H-5*a*), 3.85 (t, $^3J_1 = {}^3J_2 = 7.7$, H-24), 4.18 (dd, $^2J = 11.6$, $^3J = 5.6$, β-D-xylopyranose H-5*e*), 4.75 (d, $^3J = 7.7$, β-D-xylopyranose H-1), 4.80 (td, $^3J_1 = {}^3J_2 = 10.6$, $^3J_3 = 3.5$, H-7), 5.20

(td, $^3J_1 = {}^3J_2 = 9.9$, $^3J_3 = 5.5$, β-D-xylopyranose H-4), 5.32 (dd, $^3J_1 = 9.4$, $^3J_2 = 7.5$, β-D-xylopyranose H-2), 5.49 (td, $^3J_1 = {}^3J_2 = 7.7$, $^3J_3 = 4.8$, H-16), 5.59 (t, $^3J_1 = {}^3J_2 = 9.4$, β-D-xylopyranose H-3).

Table 1 lists the ^{13}C NMR spectrum.

Further elution of the column by the same solvent system produced a fraction containing a mixture of **2** and **7** (100 mg). Acetate **7** dominated the mixture.

Further elution of the column by the same solvent system gave **2** (35 mg) as described above.

2′,3′,4′,7,16-Pentaacetate of 3-*O*-β-D-Xylopyranoside-20*R*,25-*nor*-cycloartan-3β,7β,16β-triol-20,24-olide (8) from 7. Pentaacetate **7** (315 mg) in acetone (15 mL) was treated with Jones reagent (0.4 mL) [4] and stirred for 20 min at 17°C. The excess of oxidant was decomposed by adding MeOH (1 mL) to the reaction mixture. The solution was diluted with H_2O and worked up with $CHCl_3$. The $CHCl_3$ extract was washed with H_2O and evaporated. The solid was chromatographed over a column with elution by system 4 to isolate **8** (289 mg), $C_{42}H_{60}O_{14}$, mp 238–240°C (MeOH).

IR spectrum (KBr, ν_{max}, cm^{-1}): 1760 (γ-lactone), 1731, 1247 (ester).

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.20 and 0.54 (d, $^2J = 4$, 2H-19), 0.76, 0.78, 0.84, 1.22, 1.36 (s, 5 × CH_3), 1.85, 1.90, 1.91, 1.96, 2.00 (s, 5 × Ac), 2.50 (d, $^3J = 8$, H-17), 3.17 (dd, $^3J_1 = 11.7$, $^3J_2 = 4.5$, H-3), 3.54 (dd, $^2J = 11.7$, $^3J = 9.9$, β-D-xylopyranose H-5*a*), 4.19 (dd, $^2J = 11.5$, $^3J = 5.4$, β-D-xylopyranose H-5*e*), 4.75 (d, $^3J = 7.5$, β-D-xylopyranose H-1), 4.77 (td, $^3J_1 = {}^3J_2 = 11$, $^3J_3 = 4$, H-7), 5.20 (td, $^3J_1 = {}^3J_2 = 9.8$, $^3J_3 = 5.6$, β-D-xylopyranose H-4), 5.32 (dd, $^3J_1 = 9.4$, $^3J_2 = 7.5$, β-D-xylopyranose H-2), 5.50 (td, $^3J_1 = {}^3J_2 = 8$, $^3J_3 = 6$, H-16), 5.59 (t, $^3J_1 = {}^3J_2 = 9.4$, β-D-xylopyranose H-3).

Table 2 lists the ^{13}C NMR spectrum.

3-*O*-β-D-Xylopyranoside-20*R*,25-*nor*-cycloartan-3β,7β,16β-triol-20,24-olide (9) from 8. Acetate **8** (269 mg) was dissolved in methanolic NaOH (16 mL, 1%), left at 17°C for 16 d, acidified with methanolic H_2SO_4 (2.5%), and diluted with H_2O. The MeOH was evaporated. The aqueous solution was treated with *n*-BuOH. The BuOH extract was washed with H_2O and evaporated to dryness. The solid was chromatographed over a column with elution by system 5 to isolate **9** (116 mg), $C_{32}H_{50}O_9$, mp 276–278°C (EtOH).

IR spectrum (KBr, ν_{max}, cm^{-1}): 3515–3455 (OH), 3031 (cyclopropane CH_2), 1756 (γ-lactone).

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.17 and 0.62 (d, $^2J = 4.2$, 2H-19), 0.94, 0.96, 1.21, 1.38, 1.45 (s, 5 × CH_3), 1.85 (d, $^3J = 9.6$, H-8), 2.44 (d, $^3J = 8.4$, H-17), 3.27 (td, $^2J = {}^3J_1 = 12.2$, $^3J_2 = 10.2$, H-22), 3.39 (dd, $^3J_1 = 11.8$, $^3J_2 = 4.4$, H-3), 3.64 (dd, $^2J = 10.9$, $^3J = 10$, β-D-xylopyranose H-5*a*), 3.64 (td, $^3J_1 = {}^3J_2 = 10$, $^3J_3 = 4$, H-7), 3.92 (dd, $^3J_1 = 8.9$, $^3J_2 = 7.6$, β-D-xylopyranose H-2), 4.04 (t, $^3J_1 = {}^3J_2 = 8.7$, β-D-xylopyranose H-3), 4.12 (td, $^3J_1 = {}^3J_2 = 8.7$, $^3J_3 = 5.1$, β-D-xylopyranose H-4), 4.26 (dd, $^2J = 11$, $^3J = 5.1$, β-D-xylopyranose H-5*e*), 4.74 (d, $^3J = 7.6$, β-D-xylopyranose H-1), 4.78 (td, $^3J_1 = {}^3J_2 = 8$, $^3J_3 = 7$, H-16).

Table 2 lists the ^{13}C NMR spectrum.

20*R*,24*S*-Epoxy-19(10→9)-*abeo*-lanosta-1(10),7-dien-3β,16β,25-triol (11) from 10. Cycloalpigenin D (**10**, 200 mg) in Py (2 mL) was treated with benzenesulfonylchloride (0.7 mL), left at room temperature for 24 h, and poured onto ice. The resulting precipitate was filtered off, washed with H_2O, and dried. The solid was chromatographically homogeneous. The solid was recrystallized from EtOH to afford **11**, $C_{30}H_{48}O_4$, mp 170–172°C.

PMR spectrum (400 MHz, C_5D_5N, δ, ppm, J/Hz, 0 = HMDS): 0.79, 0.92, 1.01, 1.16, 1.21, 1.28, 1.29, 1.40 (s, 8 × CH_3), 2.28 (m, H-2), 2.35 (d, $^3J = 7.4$, H-17), 2.54 (dt, $^2J = 17.8$, $^3J_1 = {}^3J_2 = 5.2$, H-2), 2.95 (q, $^2J = {}^3J_1 = {}^3J_2 = 10.4$, H-22), 3.67 (dd, $^3J_1 = 9.8$, $^3J_2 = 5.8$, H-3), 3.75 (dd, $^3J_1 = 8.8$, $^3J_2 = 4.6$, H-24), 4.95 (td, $^3J_1 = {}^3J_2 = 7.7$, $^3J_3 = 5.9$, H-16), 5.46 (dd, $^3J_1 = 4.5$, $^3J_2 = 2.2$, H-1 and H-7).

Table 2 lists the ^{13}C NMR spectrum.

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REFERENCES

1. M. I. Isaev, M. B. Gorovits, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 156 (1989).
2. Jpn. Pat. No. 59,36,623 (1984); *Ref. Zh. Khim.*, 1985, 5O233P.
3. M. I. Isaev, M. A. Agzamova, Z. A. Khushbaktova, Yu. R. Mirzaev, V. N. Syrov, M. B. Gorovits, and N. K. Abubakirov, USSR Pat. No. 1,540,245; MKI^3 A 61 K 31/585, C 07 J 17/00.
4. C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).
5. M. I. Isaev, *Khim. Prir. Soedin.*, 710 (1991).
6. R. P. Mamedova, M. A. Agzamova, and M. I. Isaev, *Khim. Prir. Soedin.*, 453 (2001).
7. M. A. Agzamova and M. I. Isaev, *Khim. Prir. Soedin.*, 377 (1991).