5. A. Groweiss, Y. Kashman, D. J. Vanderah, B. Tursch, P. Cornet, J. C. Braekman, and D. Daloze, Bull. Soc. Chim. Belg., 87, 277 (1978).
6. V. A. Raldugin, N. I. Yaroshenko, and T. P. Ponomareva, Khim. Prir. Soedin., 844 (1980).
7. S. Carmely, A. Groweiss, and Y. Kashman, J. Org. Chem., 46, 4279 (1981).
8. A. Horeau, Tetrahedron Lett., 506 (1961).
9. M. G. B. Drew, P. H. Templeton, and A. Zalkin, Acta Crystallogr., B25, 261 (1969).
10. E. J. Corey and K. Achiwa, J. Org. Chem., 43, 11 (1969).
11. E. Glotter, S. Greenfield, and D. Lavie, J. Chem. Soc. (C), 1646 (1968).
12. Y. Naya, K. Yoshihara, T. Iwashita, H. Komura, K. Nakanishi, and Y. Hata, J. Am. Chem. Soc., 103, 7009 (1981).
13. N. Harada, J. Iwabuchi, Y. Yokota, H. Uda, and K. Nakanishi, J. Am. Chem. Soc., 103, 5590 (1981).

TRITERPENE GLYCOSIDES OF Astragalus AND THEIR GENINS.

XXVII. X-RAY STRUCTURAL INVESTIGATION OF CYCLOGALEGIGENIN

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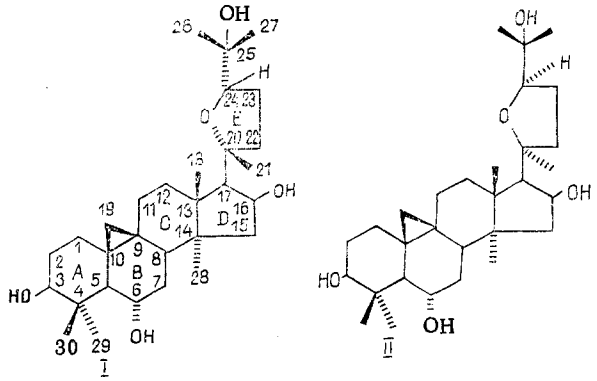
It has been shown by x-ray structural analysis that cyclogalegigenin has the 20S,24R stereochemistry and, consequently, is 20S,24R-epoxycycloartane-3β,-6α,16β,25-tetraol. Cyclosieversigenin is 20R,24S-epoxycycloartane-3β,6α,16β,-25-tetraol.

Cyclosieversigenin (I) and cyclogalegigenin (II) are genins of the cycloartane series of similar structure that have been isolated from various species of Astragalus [1-4].



Cyclosieversigenin was previously ascribed the structure of 20S,24R-epoxycycloartane-3β,6α,16β,25-tetraol [1]. On the basis of spectral characteristics, and also of chemical transformations permitting a correlation to be made of its structure with that of cyclosieversigenin, cyclogalegigenin was characterized as 20R,24S-epoxycycloartane-3β,6α,16β,25-tetraol [4]. It can be seen from this that these two genins differ only by the configurations of the C20 and C24 chiral centers. In the present paper we give the results of an x-ray structural analysis of cyclogalegigenin (II), which has permitted the stereochemistry of the C20 and C24 atoms to be defined more accurately.

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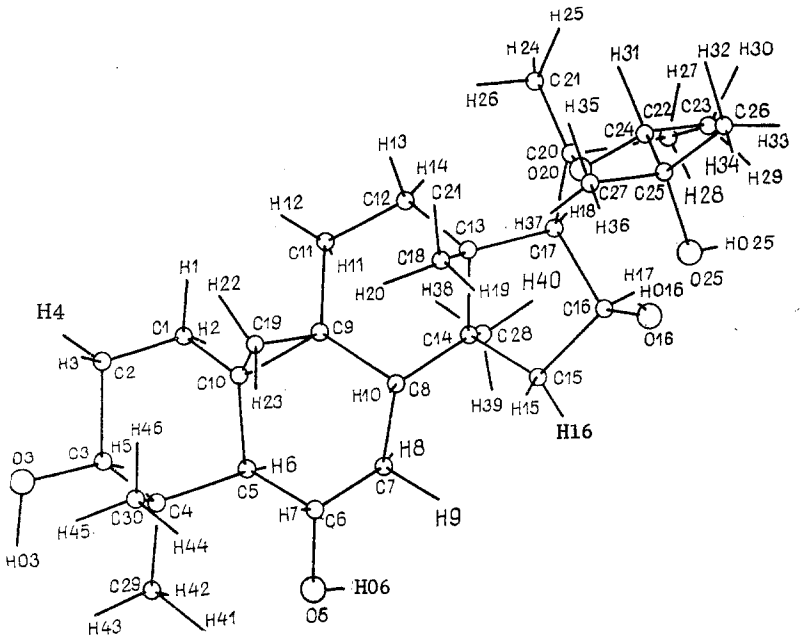

Fig. 1. Structure of the molecule in a projection on the mean plane of the steroid nucleus.

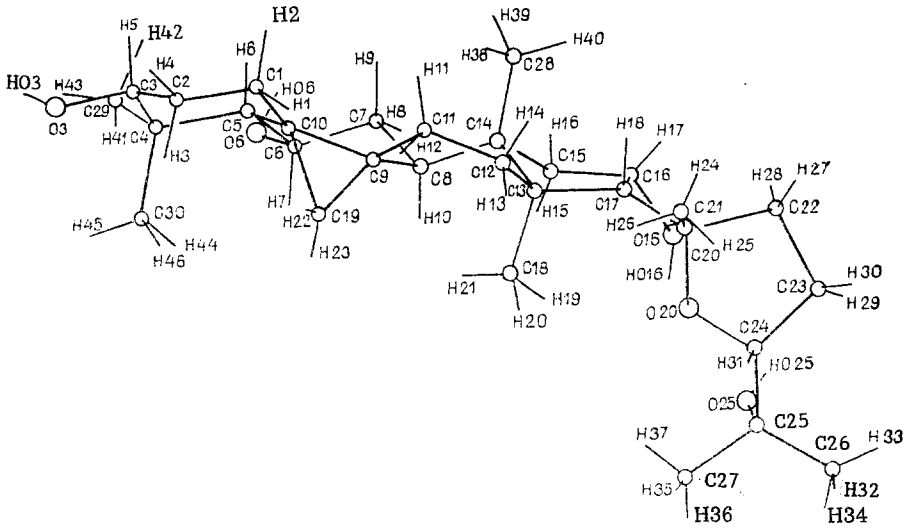

Fig. 2. Structure of the molecule in a projection on the mean plane of ring E.

The structure of the molecule of (II) in two projections [5] is shown in Figs. 1 and 2. As can be seen from these figures, the steroid nucleus of the molecule in the system of coordinates used (see Experimental) has the standard chirality for steroids [5], which permits the required configuration to be ascribed unambiguously to the asymmetric centers C20 and C24: in contrast to the original proposals [4], cyclogalegigenin has not the 20R,24S but the 20S,24R stereoconfiguration. The interatomic distances in its molecule (Table 1) agree, in the main, with the length of the corresponding bonds in related compounds [6-8]. The lengths of the $C(sp^3)$–$C(sp^3)$ bonds lie within the interval of 1.475-1.579 Å. The lengths of the shortest of these bonds – C24–C25, C1–C10, and C1–C2 are 1.475, 1.486, and 1.492 Å, respectively. The extra- and intracyclic C–O interatomic distances, with the exception of the C16–O16 bond, are, when the error of their determination is allowed for, actually identical (1.432-1.454 Å) and correspond to the standard length of an ordinary bond. The C16–O16 distance is somewhat shorter at 1.396 Å.

TABLE 1. Interatomic Distances (R, Å) and Main Valence Angles* (ω, deg) in the Cyclogalegigenin Molecule

Atom	R	Atom	R	Atom	R
O3 — C3	1,438(7)	C5 — C10	1,543(6)	C13 — C18	1,533(8)
O6 — C6	1,432(5)	C6 — C7	1,523(6)	C14 — C15	1,508(8)
O16 — C16	1,396(8)	C7 — C8	1,520(6)	C14 — C28	1,551(8)
O20 — C20	1,437(6)	C8 — C9	1,539(8)	C15 — C16	1,542(7)
O20 — C24	1,454(6)	C8 — C14	1,538(6)	C16 — C17	1,554(8)
O25 — C25	1,446(6)	C9 — C10	1,544(8)	C17 — C20	1,552(7)
C1 — C2	1,492(9)	C9 — C11	1,534(8)	C20 — C21	1,522(9)
C1 — C10	1,486(10)	C9 — C19	1,517(8)	C20 — C22	1,562(7)
C2 — C3	1,540(8)	C10 — C19	1,530(10)	C22 — C23	1,504(10)
C3 — C4	1,507(10)	C11 — C12	1,565(9)	C23 — C24	1,543(7)
C4 — C5	1,579(7)	C12 — C13	1,529(9)	C24 — C25	1,475(10)
C4 — C29	1,529(7)	C13 — C14	1,561(6)	C25 — C26	1,551(9)
C4 — C30	1,540(10)	C13 — C17	1,567(7)	C25 — C27	1,543(8)
C5 — C6	1,523(8)				

Angle	ω	Angle	ω	Angle	ω
C24O20C20	109,8(4)	C1C10C9	119,5(5)	C13C17C16	104,7(4)
O3C3C2	107,9(4)	C5C10C9	121,7(5)	C13C17C20	120,0(4)
O3C3C4	111,8(5)	C1C10C19	116,6(5)	C16C17C20	114,8(5)
C2C3C4	115,2(6)	C5C10C19	120,3(5)	C9C19C10	60,9(4)
O6C6C5	112,3(4)	C9C10C19	59,1(4)	O20C20C17	109,8(4)
O6C6C7	109,0(3)	C9C11C12	116,5(6)	O20C20C21	109,0(4)
C7C8C14	114,0(4)	C11C12C13	114,6(5)	O20C20C22	103,7(5)
C8C9C10	117,2(4)	C12C13C17	116,6(4)	C20C22C23	105,8(5)
C8C9C11	118,5(4)	C14C13C17	100,9(4)	O20C24C23	103,6(4)
C8C9C19	114,1(5)	C8C14C15	113,4(4)	O20C24C25	108,7(4)
C10C9C19	60,0(4)	C13C14C15	103,2(4)	C23C24C25	118,0(5)
C11C9C19	117,0(4)	C14C15C16	105,6(4)	O25C25C24	111,8(5)
		O16C16C15	111,6(5)	O25C25C26	109,5(5)
		O16C16C17	117,4(4)	O25C25C27	104,8(4)

*The values of the C–C–C angles not given in the table lie in the 106.5-112.5° interval.

TABLE 2. Torsional Angles (φ, deg) in the Cyclogalegigenin Molecule

Angle	φ	Angle	φ
C1C2C3C4	52,8	C13C14C15C16	—37,1
C2C3C4C5	—51,1	C14C15C16C17	14,9
C3C4C5C10	53,3	C15C16C17C13	12,9
C4C5C10C1	—58,2	C16C17C13C14	—34,6
C5C10C1C2	58,4	C17C13C14C15	44,3
C10C1C2C3	—54,5	O20C20C22C23	—18,1
C5C6C7C8	70,6	C20C22C23C24	—1,0
C6C7C8C9	—53,2	C22C23C24O20	19,6
C7C8C9C10	20,6	C23C24O20C20	—33,0
C8C9C10C5	—5,2	C24O20C20C22	32,3
C9C10C5C6	20,6	C13C17C20C21	—54,8
C10C5C6C7	—51,3	C13C17C20C22	—179,1
C8C9C11C12	—33,2	C16C17C20O20	—59,6
C9C11C12C13	11,5	C16C17C20C21	179,2
C11C12C13C14	38,0	O20C24C25O25	60,1
C12C13C14C8	—71,8	C20O20C24C25	—159,3
C13C14C8C9	50,4	C22C23C24C25	139,7
C14C8C9C11	1,2	C23C24C25O25	—57,5

The conformation of the steroid nucleus of the molecule can be well seen from Fig. 2. In ring A, the C1, C2, C4, and C5 atoms are coplanar, deviating from the mean plane by not more than 0.003 Å. The C3 and C10 atoms are displaced in different directions from this plane by 0.606 and 0.680 Å. Thus, this ring has an almost ideal chair conformation. In ring B, the C5, C10, C9, and C8 atoms deviate from the plane that they determine by not more than 0.137 Å, while the C6 and C7 atoms are displaced on opposite sides of it by 0.351 and 0.353 Å, respectively. The conformation of this ring is the half-chair conformation characteristic

TABLE 3. Hydrogen Bonds

D–H...A bond	Position of A	D...A, Å	D–H, Å	H...A, Å
O3 — HO3...O6	0,5—x, —1—y, 0,5+z	2,652	1,01	1,96
O6 — HO6...O16	0,5—x, —y, 0,5+z	2,668	0,71	1,98
O25 — HO25...O3	x, y, —1+z	2,847	0,72	2,31
O16 — HO16...O20	x, y, z,	2,718	0,83	2,37
O16 — HO16...O25	x, y, z,	2,945	0,83	2,26

TABLE 4. Coordinates of the Basis Nonhydrogen Atoms ($\times 10^4$)

Atom	x	y	z	Atom	x	y	z
O3	3403 (1)	—5771 (4)	10647(6)	C14	3346 (2)	336 (4)	6735 (6)
O6	2283 (1)	—3248(3)	7248 (4)	C15	3079 (2)	752 (4)	5500 (6)
O16	3362 (1)	2112 (4)	3772 (5)	C16	3329 (2)	1942 (5)	5156 (7)
O20	4378 (1)	2150 (3)	4017 (0)	C17	3825 (2)	2021 (4)	5973 (6)
O25	4003 (1)	2326 (3)	1373 (5)	C18	4159 (2)	—1 (4)	5448 (7)
C1	3769 (2)	—2638 (6)	10133 (8)	C19	3942 (2)	—2532 (5)	7604(9)
C2	3818 (2)	—3888 (6)	10494 (9)	C20	4264 (2)	2698 (4)	5271 (6)
C3	3318 (2)	—4577 (5)	10316 (8)	C21	4735 (2)	2757 (6)	6134 (8)
C4	3076 (2)	—4461 (4)	8960 (7)	C22	4111 (2)	3947 (4)	4854 (7)
C5	3046 (2)	—3123 (4)	8625 (7)	C23	4311 (2)	4129 (4)	3457 (7)
C6	2790 (2)	—2803 (4)	7316 (6)	C24	4584 (2)	3011 (5)	3084 (7)
C7	2792 (2)	—1485 (4)	7178 (6)	C25	4524 (2)	2559 (4)	1707 (8)
C8	3318 (2)	—993 (4)	6906 (6)	C26	4760 (2)	3422 (5)	672 (8)
C9	3702 (2)	—1392 (4)	7948 (7)	C27	4776 (2)	1376 (5)	1558 (9)
C10	3564 (2)	—2500(4)	8758 (7)	C28	3107 (2)	935 (5)	7963 (7)
C11	4034 (2)	—467 (5)	8656 (8)	C29	2552 (2)	—5034 (5)	9074 (8)
C12	4187 (2)	636 (5)	7814 (8)	C30	3383 (3)	—5097 (5)	7895 (9)
C13	3901 (2)	754 (4)	6494 (6)				

for cyclohexene. The stabilization of such a conformation for this ring is due to the cyclopropane ring condensed with it at the C10—C9 bond. Ring C has a distorted boat conformation (twist form). The C8, C9, C12, and C13 atoms deviate from the plane that they determine by 0.126, —0.121, 0.122, and —0.127 Å, respectively, while the C11 and C14 atoms deviate from it by 0.269 and 0.727 Å in the same direction. Ring D has the envelope conformation. The C13, C15, C16, and C17 atoms are located in one plane to within 0.078 Å, while the C14 atom is displaced from it by 0.632 Å. The tetrahydrofuran ring E has the same conformation: The C20, C22, C23, and C24 atoms are in the same plane (the maximum deviation being 0.006 Å), while the O20 atoms deviates from it by 0.454 Å in the direction of the O16 atom. This ring is approximately perpendicular to the mean plane of the steroid nucleus, and the C21 atom is in the trans position with respect to the C16 atom. The C16C17C20C21 torsional angle is 179.2° (Table 2).

In the molecule two short intramolecular contacts can be seen: O16...O20, 2.72 Å and O16...O25, 2.95 Å. These contacts can be interpreted as a weak bifurcated hydrogen bond which apparently plays an important role in the stabilization of the conformation of the molecule. The proton donor in this bond is the hydroxy group at the C16 atom.

In the crystal, the molecules are linked with one another by a system of O—H...O hydrogen bonds in which two hydroxy groups participate (Table 3). The molecules linked by the hydrogen bonds form a layer perpendicular to the a axis. Between such layers only a van der Waals interaction exists, which explains the pronounced cleavability of the crystals perpendicularly to the a axis. It must be mentioned that the observed system of intermolecular and intramolecular hydrogen bonds fully saturates the donor—acceptor capacity of all the hydroxy groups of the molecule for the formation of such bonds. Each of these groups participates in two hydrogen bonds, acting simultaneously as proton donor and proton acceptor.

Thus, cyclogalegigenin is of the structure 20S,24R-epoxycycloartane-3β,6α,16β,25-tetraol. As shown above, the configurations of the C20 and C24 atoms of cyclogalegigenin (II) and of cyclosieversigenin (I) are mutually opposite [4]. As our investigations have shown, (II) has the 20S,24R-stereochemistry. In this case, (I) must be described as 20R,24S-epoxycycloartane-3β,6α,16β,25-tetraol. It is quite likely that cycloastrogenol, recently isolated from Astragalus membranaceus Bunge [9] is identical with cyclosieversigenin.

EXPERIMENTAL

Single crystals of compound (II) are colorless and transparent and in the form of regular hexagonal prisms in the monoclinic system. For the x-ray structural analysis we used a specimen with dimensions of 0.25 × 0.40 × 0.50 mm. Parameters of the elementary cell: a = 26.666(9), b = 11.507(6), c = 9.970(5) Å, γ = 91.8(2)°, sp. gr. B2; z = 4; $C_{30}H_{50}O_5$.

The parameters of the elementary cell and the intensities of 2370 independent reflections with $I > 2\sigma(I)$ were measured on a DAR-UMB automatic diffractometer in Cu Kα radiation.

The structure was interpreted by the direct method using the MULTAN-78 program [10] and was refined by the MLS with allowance for the anisotropy of the thermal vibrations for the nonhydrogen atoms. All the hydrogen atoms were revealed objectively in an electron-density difference synthesis and their positions were defined by the MLS in the isotropic approximation. The positions of CH_2 and CH_3 groups were refined on the assumption that they were rigid fragments with fixed C–H distances (1.08 Å) and fixed H–C–H angles (109.5°). The final value of the divergence factor R was 5.4%. The coordinates of the atoms are given in Table 4. The calculations were made by the YANX program [11].

Since because of the absence of anomalously scattering atoms from the (II) molecule the absolute configuration cannot be determined experimentally (by a comparison of the R factors for the "direct" and the inverted structure), the absolute configuration (and the given values of the coordinates of the atoms; see Table 4) that we assigned is based on the choice of the correct chirality of the steroid nucleus shown by the torsional angles corresponding to it (see Table 2) [5].

CONCLUSIONS

It has been shown by x-ray structural analysis that cyclogalegigenin has the 20S,24R-configuration and, consequently, is 20S,24R-epoxycycloartane-3β,6α,16β,25-tetraol. Cyclosieversigenin is 20R,24S-epoxycycloartane-3β,6α,16β,25-tetraol.

LITERATURE CITED

1. A. N. Svechnikova, R. U. Umarova, M. B. Gorovits, K. L. Seitanidi, Ya. V. Rashkes, M. R. Yagudaev, and N. K. Abubakirov, Khim. Prir. Soedin., 67 (1981).
2. M. I. Isaev, M. B. Gorovits, N. D. Abdullaev, and N. K. Abubakirov, Khim. Prir. Soedin., 458 (1982).
3. R. U. Umarova, A. N. Svechnikova, N. D. Abdullaev, M. B. Gorovits, and N. K. Abubakirov, Khim. Prir. Soedin., 188 (1984).
4. M. D. Alaniya, M. I. Isaev, M. B. Gorovits, N. D. Abdullaev, É. P. Kemertelidze, and N. K. Abubakirov, Khim. Prir. Soedin., 332 (1983).
5. W. L. Duax and D. A. Norton, Atlas of Steroid Structure, Vol. 1, IFI/Plenum, New York (1975).
6. L. G. Vorontsova, Zh. Strukt. Khim., 20, 882 (1979).
7. D. C. Rohrer, Acta Crystallogr., B36, 1565 (1980).
8. A. S. Gromova, V. I. Lutskii, A. A. Semenov, E. V. Slavyanov, V. N. Biyushkin, and T. I. Malinovskii, Khim. Prir. Soedin., 718 (1982).
9. I. Kitagawa, H. K. Wang, A. Tagaki, M. Fuchida, I. Miura, and M. Yoshikawa, Chem. Pharm. Bull., 31, 689 (1983).
10. P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declerco, and M. M. Woolfson, MULTAN-78, Universities of York, England and Louvain, Belgium (1978).
11. R. G. Geer, A. I. Yanovskii, and Yu. T. Struchkov, Kristallografiya, 28, 1029 (1983).