CRYSTAL AND MOLECULAR STRUCTURE OF 3β-ACETOXY-22S,25-EPOXYHOLOSTA-7,9(11)-DIEN-17α-OL

S. G. Il'in, M. V. Reshetnyak, G. K. Oleinikova, and Yu. T. Struchkov

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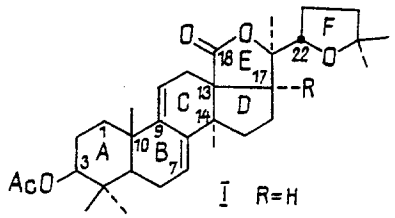
A complete x-ray structural investigation has been made of 3β-acetoxy-22S,25-epoxyholosta-7,9(11)-dien-17α-ol. Important conformational differences between this compound and its 17-deoxy derivative have been found which show the mobility of the conformation of rings B and C of the holostane series and the tetrahydrofuran ring of the side chain of the molecule. It has been shown that the conformation of the side chain of the molecule is stabilized by an O17–H...O22 intramolecular hydrogen bond, without excluding the possibility of the participation of the hydroxy group in the formation of intermolecular hydrogen bonds (bifurcated).

Triterpene glycosides of holothurians possessing various physiological activities [1-3] are attracting the attention of researchers also by virtue of their interesting stereochemical features [4-6]. Aglycons of types (I) and (II) with a heteroanular system of double bonds in rings B and C are obtained in the acid hydrolysis of glycosides having native genins with the 9(11) position of double bond and a 12α-OH group [7, 8]. We have investigated the spatial structure of the acetate of



17-deoxy-22,25-epoxyholothurinogenin (I) previously [9]. However, confirmation of features of genins of type (II) containing a 17α-OH group remained obscure. In order to establish the stereochemical features of genins of this type we have made an x-ray structural investigation of 3β-acetoxy-22S,25-epoxyholosta-7,9(11)-dien-17α-ol (II).

The spatial structure of the (II) molecule is given in Fig. 1. The conformations of the rings in compounds (II) are as follows: A – chair; B – 5α,10β-half-chair distorted in the direction of a 5α-sofa; C – 13β-sofa distorted in the direction of a 13β,14α-half-chair; D – 14α-envelope; E – 17β-envelope; and F – 22,23-half-chair. Ring linkages: A/B – trans;

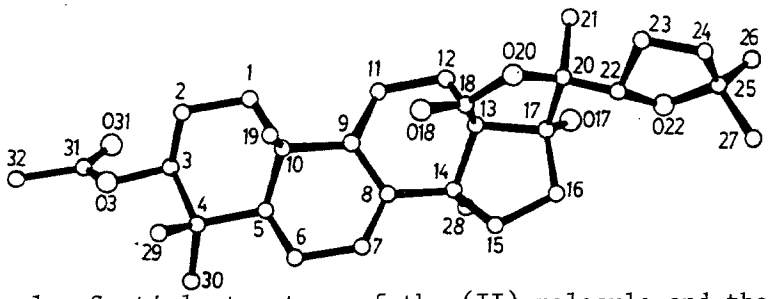


Fig. 1. Spatial structure of the (II) molecule and the numbering of the atoms.

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TABLE 1. Bond Lengths, d (Å), and Valence Angles, ω (°)

Bond	d	Angle	ω	Angle	ω
C1—C2	1,525 (8)	C2—C1—C10	112,8 (4)	C15—C16—C17	108,3 (4)
C1—C10	1,537 (7)	C1—C2—C3	111,2 (5)	C13—C17—C16	102,6 (3)
C2—C3	1,412 (8)	C2—C3—C4	110,2 (4)	C13—C17—C20	103,3 (3)
C3—C4	1,676 (7)	C2—C3—O3	114,5 (5)	C13—C17—O17	111,1 (3)
C3—O3	1,454 (6)	C4—C3—O3	101,2 (4)	C16—C17—C20	116,4 (4)
C4—C5	1,558 (7)	C3—C4—C5	105,4 (4)	C16—C17—O17	111,9 (4)
C4—C29	1,544 (8)	C3—C4—C29	111,1 (4)	C20—C17—O17	110,9 (4)
C4—C30	1,529 (9)	C3—C4—C30	108,5 (4)	C13—C18—O18	111,5 (3)
C5—C6	1,543 (6)	C5—C4—C29	114,1 (4)	C13—C18—O20	128,4 (4)
C5—C10	1,557 (6)	C5—C4—C30	109,3 (4)	O18—C18—O20	120,1 (4)
C6—C7	1,501 (8)	C29—C4—C30	108,4 (5)	C17—C20—C21	113,2 (4)
C7—C8	1,344 (7)	C4—C5—C6	113,0 (4)	C17—C20—C22	113,6 (4)
C8—C9	1,456 (6)	C4—C5—C10	118,9 (4)	C17—C20—O18	102,7 (3)
C8—C14	1,512 (6)	C6—C5—C10	109,3 (4)	C21—C20—C22	111,3 (4)
C9—C10	1,536 (6)	C5—C6—C7	111,6 (4)	C21—C20—O18	109,6 (4)
C9—C11	1,348 (6)	C6—C7—C8	122,9 (4)	C22—C20—O18	105,7 (4)
C10—C19	1,548 (7)	C7—C8—C9	121,8 (5)	C20—C22—C23	117,6 (5)
C11—C12	1,547 (8)	C7—C8—C14	120,8 (4)	C20—C22—O22	106,2 (4)
C12—C13	1,486 (6)	C9—C8—C14	116,7 (4)	C23—C22—O22	105,1 (4)
C13—C14	1,535 (6)	C8—C9—C10	117,2 (4)	C22—C23—C24	102,4 (5)
C13—C17	1,562 (5)	C8—C9—C11	120,4 (4)	C23—C24—C25	109,2 (6)
C13—C18	1,523 (6)	C10—C9—C11	122,4 (4)	C24—C25—C26	120,4 (8)
C14—C15	1,529 (6)	C1—C10—C5	109,6 (4)	C24—C25—C27	109,1 (9)
C14—C28	1,539 (6)	C1—C10—C9	111,8 (4)	C24—C25—O22	106,6 (5)
C15—C16	1,551 (8)	C1—C10—C19	108,6 (4)	C26—C25—C27	102,3 (8)
C16—C17	1,537 (6)	C5—C10—C9	106,9 (4)	C26—C25—O22	109,1 (6)
C17—C20	1,548 (6)	C5—C10—C19	114,0 (4)	C27—C25—O22	109,0 (7)
C17—O17	1,424 (5)	C9—C10—C19	106,1 (4)	C32—C31—O3	110,9 (5)
C18—O18	1,342 (5)	C9—C11—C12	125,6 (4)	C32—C31—O31	123,6 (5)
C18—O20	1,205 (4)	C11—C12—C13	109,4 (4)	O3—C31—O31	125,5 (5)
C20—C21	1,518 (7)	C12—C13—C14	113,9 (3)	C3—O3—C31	113,3 (4)
C20—C22	1,536 (7)	C12—C13—C17	120,1 (3)	C18—O18—C20	111,4 (3)
C20—O18	1,459 (6)	C12—C13—C18	104,4 (3)	C22—O22—C25	109,4 (4)
C22—C23	1,527 (7)	C14—C13—C17	105,7 (3)		
C22—O22	1,413 (6)	C14—C13—C18	113,4 (3)		
C23—C24	1,441 (9)	C17—C13—C18	98,5 (3)		
C24—C25	1,44 (1)	C8—C14—C13	111,3 (3)		
C25—C26	1,42 (1)	C8—C14—C15	118,8 (4)		
C25—C27	1,46 (2)	C8—C14—C28	106,0 (4)		
C25—O22	1,426 (7)	C13—C14—C15	101,3 (3)		
C31—C32	1,517 (8)	C13—C14—C28	110,7 (3)		
C31—O3	1,317 (6)	C15—C14—C28	108,8 (4)		
C31—O31	1,192 (7)	C14—C15—C16	104,5 (4)		

B/C – planar; C/D – trans; D/E – cis. The conformations of rings A, D, and E and the nature of the linkage of the rings in compounds (I) and (II) coincide. However, in the (I) molecule rings B and C have the 5α-sofa and the 13β,14α-half-chair conformations. The differences in the conformations of rings B and C in compounds (I) and (II) may be a consequence of a difference in the packing of the molecules in the crystals of these compounds but may also be the result of the conformational transition of steric stresses arising in the presence of the 17α-OH group. Such stresses in (II) exist between the 17α-OH group and the methyl groups in positions 14α (the O17...C28 distance is 3.08 Å) and 20α (the O17...C21 distance is 2.76 Å), and also between the hydroxy group and the C12 atom (the O17...C12 distance is 2.98 Å). In any case, these differences show a conformational mobility of rings B and C in triterpenes of such structure. The conformations of rings F in compounds (I) and (II) also differ considerably [in compound (I), ring F has a 25,022-half-chair conformation].

In view of the presence of the lactone ring E in triterpenoids of the holostane series, it is convenient to define the conformations of the side chains in Klyne and Prelog's terms [10], starting from the values of the C17–C20–C22–C23 torsional angle. In compounds (I) and (II) the values of this angle are 174 and 176°C and, consequently, the conformations of the side chains are +antiperiplanar. In compound (II) the conformation of the side chain is stabilized by an O17–H...O22 hydrogen bond with a O...O distance of 3.08 Å (the O–H...O22 angle is 122°). In the crystals of compound (II) we detected a weak O17–H...O31' intermolecular hydrogen bond with an O...O distance of 3.15 Å (the O17–H...O31' angle being 149°). Thus, the hydrogen atom of the hydroxy group participates in the formation of a bifurcated hydrogen bond: intramolecularly with the O22 atom and intermolecularly with the oxygen atom of the acetyl group.

TABLE 2. Coordinates of the Nonhydrogen Atoms ($\times 10^4$) and Equivalent Isotropic Thermal Parameters ($Å^2 \times 10^3$)

Atom	x/a	y/b	z/c	U_{eq}
C1	8309 (6)	6954 (4)	1400 (2)	47 (1)
C2	8519 (6)	7546 (4)	1843 (2)	52 (1)
C3	7585 (6)	8421 (4)	1790 (2)	49 (1)
C4	5372 (7)	8226 (4)	1742 (2)	53 (1)
C5	5191 (6)	7538 (3)	1319 (1)	45 (1)
C6	3234 (6)	7214 (4)	123 (2)	61 (1)
C7	3 83 (6)	6628 (4)	796 (2)	52 (1)
C8	4513 (6)	6227 (3)	586 (2)	42 (1)
C9	6307 (6)	6263 (3)	788 (1)	40 (1)
C10	6463 (6)	6648 (3)	1284 (2)	43 (1)
C11	7736 (6)	5919 (3)	553 (2)	43 (1)
C12	7650 (6)	5347 (3)	5 (2)	43 (1)
C13	5757 (5)	5030 (3)	2 (1)	37 (1)
C14	4380 (5)	5463 (3)	95 (1)	41 (1)
C15	2634 (6)	5380 (4)	−62 (2)	51 (1)
C16	3183 (6)	4778 (4)	−491 (2)	56 (1)
C17	5230 (6)	4621 (3)	−476 (1)	42 (1)
C18	5469 (6)	4166 (3)	299 (1)	44 (1)
C19	5029 (7)	5800 (4)	1604 (2)	62 (1)
C20	5880 (7)	3562 (3)	−439 (2)	49 (1)
C21	7842 (7)	3433 (4)	−572 (2)	67 (1)
C22	4668 (7)	2840 (3)	−695 (2)	53 (1)
C23	5290 (9)	1791 (4)	−718 (2)	85 (3)
C24	4680 (20)	1496 (5)	−1169 (2)	133 (4)
C25	4470 (9)	2335 (5)	−1456 (2)	123 (3)
C26	5300 (20)	2476 (6)	−1844 (3)	199 (4)
C27	2680 (20)	2320 (9)	−1665 (3)	253 (5)
C28	4746 (7)	6742 (3)	− 216 (2)	54 (1)
C29	4563 (8)	7820 (5)	2193 (2)	77 (1)
C30	4442 (8)	9184 (5)	1633 (2)	77 (1)
C31	8877 (7)	9701 (4)	2198 (2)	62 (1)
C32	8960 (9)	10246 (5)	2652 (2)	91 (3)
O3	7620 (4)	9031 (2)	2210 (1)	58 (1)
O17	6125 (5)	5109 (2)	−843 (1)	58 (1)
O18	5350 (5)	3353 (2)	51 (1)	57 (1)
O20	5142 (5)	4123 (2)	706 (1)	60 (1)
O22	4615 (5)	3153 (2)	−1159 (1)	61 (1)
O31	9852 (6)	9858 (3)	1880 (1)	91 (1)

The bond lengths and valence angles in compound (II) are given in Table 1. The lengths of the bonds with the C24, C25, C26, and C27 atoms are shorter than usual because of the large thermal vibrations of these atoms.

EXPERIMENTAL

The acetate (II) ($C_{32}H_{46}O_6$) was obtained from the total glycoside fraction of Holothuria atra by known methods [11]. Crystals of compound (II) belonging to the rhombic system were grown from solutions in hexane–ethyl acetate. Space group $P2_12_12_1$, Z = 4; a = 7.428(2), b = 13.865(3), c = 28.959(6) Å, V = 2980.5 $Å^3$, d_{calc} = 1.17 g/cm^3. The integral intensities of 2837 independent reflections were measured on a CAD4 diffractometer (MoKα radiation, graphite monochromator, θ/ω method of scanning with a ratio of the scanning rates of 1.2/1). In the calculation of the intensities, corrections for the Lorentz and polarization factors were introduced into the structural factors. The structure was determined by the direct method and was refined by the method of least square in the full-matrix anisotropic approximation to R = 0.046 [1788 reflections with $I > 5\sigma(I)$]. The positional and thermal parameters of the hydrogen atoms were not refined. All the calculations were made on a PDP-11/23 computer by the SDP-PLUS programs [12]. The coordinates of the C and O atoms and their equivalent thermal parameters are given in Table 2.

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MASS SPECTRA OF ALLIOSTEROL AND ITS DEHYDRATION PRODUCT AND OF ALLOSIDES A AND B

Yu. M. Mil'grom, Ya. V. Rashkes, and S. D. Kravets

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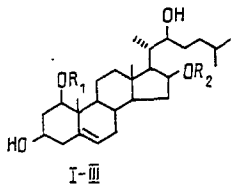
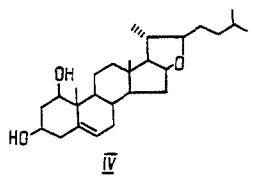
The EI and LSIMS mass spectra of alliosterol and its dehydration product and of allosides A and B have been studied. The spectra of alliosterol show features characteristic for sterols of the cholestane series. A comparison of the B/E spectra of some fragments of the ions from alliosterol and its dehydro product has shown the unimportance of the conversion of the former into the latter under mass-spectrometric conditions.

Recently, sterol glycosides (allosides A and B) the glycons of which are genetically connected with the spirostanols characteristic of these plants have been isolated from the collective fruit of the co-cultivated Allium suvorovii Rgl. and Allium stipitatum Rgl. [1]. The acid hydrolysis of allosides A (I) and B (II) formed a mixture of the corresponding aglycon – cholest-5-ene-1β,3β,16β,22-tetrol (III) and the product of its dehydration (IV), having a furostan skeleton [1]:



I-III



IV

I. R_1=H; R_2=β-D-Galp
II. R_1=β-*D*-Glcp; R_2=β-*D*-Galp
III. R_1=R_2=H

Interest in obtaining more comprehensive mass-spectrometric information than was given in [1] is due to a number of factors: the positions of the hydroxy groups, unusual for phytosterols, the probability of the (III) → (IV) transition under thermal conditions or in the dissociation of ions, and the possibility of comparing EI and LSIMS spectra and characterizing the fragmentation of compounds of the furostan series without OH groups at C-22 and C-26 (IV). The mass numbers and relative intensities of the main ions in the EI and LSIMS spectra are given in Table 1.

Institute of Chemistry of Plant Substances, Uzbekistan Academy of Sciences, Tashkent.
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