CRYSTAL AND MOLECULAR STRUCTURE OF (25R)-SPIROST-5-ENE-3β,17α-DIOL 3,17-DIACETATE (PENNOGENIN DIACETATE)

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An x-ray structural investigation has been made of pennogenin diacetate (diffractometer, direct method, anisotropic refinement, R factor 0.050). The spatial structure of the molecule has been established. The acetylation of the hydroxy group in position 17α in pennogenin is connected with the steric hindrance arising between the atoms of the acetoxy group and the atoms of ring D.

An investigation of the ^{13}C and ^{1}H NMR spectra of (25R)-spirost-5-ene-3β,17α-diol (pennogenin) and of pennogenin diacetate (I) has revealed anomalously large effects of the acetylation of the 17α-OH group [1]. The peculiarity of the NMR spectra of (I) that has been detected is apparently a reflection of structural deformations in the D–E ring system which take place on the introduction of a 17α-O-acetyl group. The influence of this substituent on the molecular conformation of steroids has been shown previously in the progesterone series [2]. The strain of the structure of pennogenin diacetate is also indicated by its chemical properties; the 17-OAc group is readily eliminated under the action of various reagents in an acid medium [3].

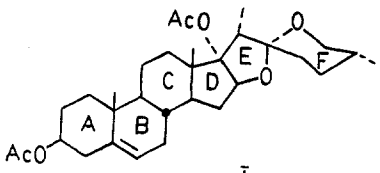

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TABLE 1. Some Torsional Angles φ (degrees)

Angle	φ	Angle	φ
C10–C1–C2–C3	–55,4(6)	C13–C14–C15–C16	–36,8(5)
C2–C1–C10–C5	48,5(6)	C14–C15–C16–C17	15,6(5)
C1–C2–C3–C4	57,6(6)	C14–C15–C16–O16	129,4(4)
C2–C3–C4–C5	–56,8(6)	C15–C16–C17–C13	11,3(5)
C2–C3–O3–C28	156,1(4)	O16–C16–C17–C13	–105,8(4)
C3–C4–C5–C10	51,8(6)	O16–C16–C17–C20	19,7(5)
C4–C5–C6–C7	–178,4(5)	C17–C16–O16–C22	–39,4(5)
C10–C5–C6–C7	2,1(8)	C16–C17–C20–C22	5,4(5)
C4–C5–C10–C1	–46,2(6)	O17–C17–C20–C21	14,2(6)
C6–C5–C10–C9	14,3(7)	C13–C17–O17–C30	–88,4(6)
C5–C6–C7–C8	13,9(7)	C17–C20–C22–O16	–28,9(5)
C6–C7–C8–C9	–44,7(6)	C21–C20–C22–O22	–41,0(6)
C7–C8–C9–C10	63,1(5)	O22–C22–C23–C24	–55,0(6)
C14–C8–C9–C11	–47,5(6)	C20–C22–O16–C16	43,3(5)
C9–C8–C14–C13	56,5(6)	O22–C22–O16–C16	–71,8(5)
C8–C9–C10–C5	–46,4(6)	C23–C22–O22–C26	57,3(6)
C8–C9–C11–C12	48,8(6)	C22–C23–C24–C25	53,6(6)
C9–C11–C12–C13	–54,1(6)	C23–C24–C25–C26	–52,2(6)
C11–C12–C13–C14	57,6(6)	C23–C24–C25–C27	–175,1(5)
C12–C13–C14–C8	–62,2(5)	C24–C25–C26–O22	54,6(6)
C17–C13–C14–C15	43,8(5)	C25–C26–O22–C22	–58,4(6)
C14–C13–C17–C16	–33,7(5)	O28–C28–O3–C3	–0,1(6)
C18–C13–C17–C20	–32,2(6)	O30–C30–O17–C17	4,6(9)

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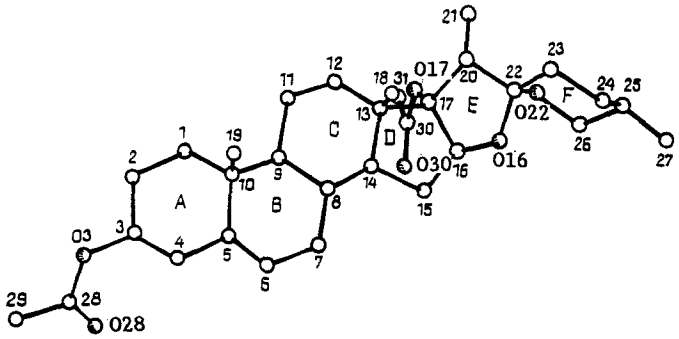

Fig. 1. Spatial structure of pennogenin diacetate.

TABLE 2. Bond Lengths d (Å) and Valence Angles (ω, degrees)

Bond	d	Angle	ω	Angle	ω
C1—C2	1,539(8)	C2—C1—C10	115,1(4)	C16—C17—C17	114,6(4)
C1—C10	1,534(7)	C1—C2—C3	109,4(5)	C20—C17—O17	104,7(4)
C2—C3	1,508(8)	C2—C3—C4	111,0(5)	C17—C20—C21	117,2(4)
C3—C4	1,504(8)	C2—C3—O3	106,3(4)	C17—C20—C22	103,0(4)
C3—O3	1,448(6)	C4—C3—O3	111,1(4)	C21—C20—C22	116,4(4)
C4—C5	1,505(7)	C3—C4—C5	112,2(4)	C20—C22—C23	115,4(5)
C5—C6	1,318(7)	C4—C5—C6	121,1(5)	C20—C22—O16	104,7(4)
C5—C10	1,537(7)	C4—C5—C10	115,4(4)	C20—C22—O22	107,1(4)
C6—C7	1,479(7)	C6—C5—C10	123,5(5)	C23—C22—O16	107,8(4)
C7—C8	1,534(8)	C5—C6—C7	124,7(5)	C23—C22—O22	111,0(4)
C8—C9	1,535(7)	C6—C7—C8	112,4(4)	O16—C22—O22	110,6(4)
C8—C14	1,524(7)	C7—C8—C9	109,0(7)	C22—C23—C24	110,8(5)
C9—C10	1,537(7)	C7—C8—C14	110,5(4)	C23—C24—C25	110,8(4)
C9—C11	1,531(8)	C9—C8—C14	109,1(4)	C24—C25—C26	108,8(5)
C10—C19	1,551(8)	C8—C9—C10	111,9(4)	C24—C25—C27	113,8(5)
C11—C12	1,530(7)	C8—C9—C11	112,8(4)	C26—C25—C27	109,9(5)
C12—C13	1,525(7)	C10—C9—C11	112,9(4)	C25—C26—O22	113,3(5)
C13—C14	1,540(7)	C1—C10—C5	109,2(4)	C29—C28—O3	111,1(5)
C13—C17	1,540(7)	C1—C10—C9	109,0(4)	C29—C28—O28	125,8(6)
C13—C18	1,535(7)	C1—C10—C19	110,0(4)	O3—C28—O28	123,1(5)
C14—C15	1,543(7)	C5—C10—C9	109,2(4)	C31—C30—O17	110,1(5)
C15—C16	1,534(7)	C5—C10—C19	108,1(4)	C31—C30—O30	124,8(5)
C16—C17	1,532(7)	C9—C10—C19	111,3(4)	O17—C30—O30	125,1(5)
C16—O16	1,434(6)	C9—C11—C12	114,9(5)	C3—O3—C28	117,2(4)
C17—C20	1,561(7)	C11—C12—C13	110,0(4)	C16—O16—C22	105,5(4)
C17—O17	1,466(6)	C12—C13—C14	107,2(4)	C17—O17—C30	126,7(4)
C20—C21	1,519(7)	C12—C13—C17	117,2(4)	C22—O22—C26	113,0(4)
C20—C22	1,522(7)	C12—C13—C18	109,8(4)		
C22—C23	1,505(8)	C14—C13—C17	101,8(4)		
C22—O16	1,425(6)	C14—C13—C18	110,5(4)		
C22—O22	1,412(6)	C17—C13—C18	110,0(4)		
C23—C24	1,530(8)	C8—C14—C13	114,6(4)		
C24—C25	1,511(8)	C8—C14—C15	118,6(4)		
C25—C26	1,502(8)	C13—C14—C15	103,2(4)		
C25—C27	1,506(8)	C14—C15—C16	103,4(4)		
C26—O22	1,436(7)	C15—C16—C17	107,6(4)		
C28—C29	1,484(8)	C15—C16—O16	110,0(4)		
C28—O3	1,350(7)	C17—C16—O16	104,9(4)		
C28—O28	1,175(8)	C13—C17—C16	105,1(4)		
C30—C31	1,478(8)	C13—C17—C20	118,7(4)		
C30—O17	1,336(7)	C13—C17—O17	110,4(4)		
C30—O30	1,197(7)	C16—C17—C20	103,9(4)		

In order to elucidate the stereochemical features of (I) we have performed an x-ray structural study of single crystals of this compound. Figure 1 illustrates the spatial structure of the molecule. Table 1 gives the values of the torsional angles characterizing the conformation of the molecule. Table 2 gives the values of the bond lengths and valence angles in the molecule. The linkage in the rings of (I) agrees with that of the Δ^5-spirostan steroids (A/B – quasi-trans; B/C and C/D – trans; D/E – cis; E/F – spiro). The values of the endocyclic torsional angles show that the (I) molecule has rings A, C, and F in the chair conformation and rings B and D in the half-chair conformation (8β,9α- and 13β,14α-, respectively). The conformation of an O16β-envelope has been found for ring E. The conformation of ring D in the (I) molecule differs from that observed in the crystal of 3β-acetoxy-(25R)-5α-spirostan-12-one in the molecule of which ring D has the conformation of a 14α-envelope [4].

TABLE 3. Coordinates of the Nonhydrogen Atoms (×10⁴)

Atom	x	y	z	Atom	x	y	z
C1	−421(9)	−8245(3)	−63(3)	C20	999(8)	−6294(2)	−3333(2)
C2	−480(9)	−8790(3)	457(3)	C21	1584(9)	−5568(3)	−3237(3)
C3	−2301(8)	−9203(2)	379(3)	C22	239(8)	−6482(3)	−3993(3)
C4	−2398(8)	−9511(3)	−277(3)	C23	1774(8)	−6532(3)	−4486(3)
C5	−2293(8)	−8994(2)	−800(2)	C24	849(10)	−6779(3)	−5173(3)
C6	−2607(8)	−8974(3)	−1254(2)	C25	−505(9)	6220(3)	−5334(3)
C7	−3589(8)	−8496(3)	−1800(2)	C26	−1915(8)	−6090(3)	−4799(3)
C8	−1632(8)	−8134(2)	−1867(2)	C27	−1599(11)	−6357(3)	−5945(3)
C9	−951(8)	−7906(2)	−1202(2)	C28	−3943(10)	−9981(3)	1058(3)
C10	−580(7)	−8502(2)	−753(2)	C29	−3543(10)	−10506(3)	1552(3)
C11	766(9)	−7418(3)	−1231(3)	C30	−3308(9)	−5897(3)	−2418(3)
C12	510(9)	−6832(2)	−1760(2)	C31	−3611(9)	−5207(3)	−2182(3)
C13	21(7)	−7698(2)	−2364(2)	O3	−2233(6)	−9713(2)	871(2)
C14	−1836(7)	−7752(3)	−2300(2)	O16	−856(6)	−7079(2)	−3892(2)
C15	−2472(8)	−7630(2)	−3001(3)	O17	−144(5)	−5985(2)	−2570(2)
C16	−1968(8)	−6961(3)	−3322(2)	O22	−983(5)	−5956(2)	−4197(2)
C17	−588(8)	−6582(2)	−2974(2)	O28	−5448(6)	−9818(2)	842(2)
C18	1711(8)	−7526(3)	−2615(3)	O30	−4563(5)	−6308(2)	−2475(2)
C19	1302(9)	−8883(3)	−941(3)				

Immediate interest is presented by a comparison of the conformations of the molecule of (I) with the two conformations of the A and B molecules of pennogenin observed in crystals of its hemihydrate [5]. The considerable conformational mobility of the 5-membered rings D and E in pennogenin is probably limited in its 17α-O-acetate, as a result of which the system of linked rings D/E in (I) assumes a conformation intermediate between the two conformations observed in pennogenin but closer to the conformation in the A molecule [5].

The geometric parameters of the tertiary OAc group are distorted. As a result of the steric hindrance arising between the C30 and O30 atoms of this group and the atoms of ring D, the C17—O17—C30 angle is increased to 126.7°, which is 9.5° greater than the value of the corresponding C—O—C angle in an OAc group at C3. The van der Waals spheres of the contacting atoms C30 and C16 (distance 2.989 Å) and O30 and C16 (distance 2.831 Å) overlap most strongly. The C17—O30 distance (2.909 Å) is 0.249 Å greater than the corresponding O28...C3 distance. The O30 and C40 atoms are also in contact. The distance between them is 3.088 Å.

EXPERIMENTAL

Single crystals of (I) ($C_{31}H_{46}O_6$) were obtained by the crystallization of a chromatographically homogeneous sample from hexane—acetone. The crystals belonged to the rhombic system, space group $P2_12_12_1$, Z = 4, a = 6.875(3), b = 19.97(1), c = 20.891(9) Å, V = 2867.7 Å^3, D_{calc} = 1.19 g/cm^3. The parameters of the unit cell and the integral intensities of 1952 observed reflections were measured on a Syntex $P2_1$ automatic defractometer (Mo Kα radiation, graphic monochromator, θ/2θ scanning method, $2\theta_{max} \leq 50°$). The structure was determined by the direct method and was refined by the method of least squares in the anisotropic full-matrix approximation to R = 0.050. In the refinement we used 1610 reflections with $|F| > 4\sigma(|F|)$. The coordinates of the atoms are given in Table 3. The calculations were performed by the INEXTL program [6] on an Eclipse S-200 computer.

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