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Structure of (22*S*)-3β-Acetoxy-20-(3-isopropylisoxazolin-5-yl)-4,4,14α-trimethylpregn-8(9)-ene

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Abstract. $C_{32}H_{51}NO_3$, $M_r = 497.7$, orthorhombic, $P2_12_12_1$, $a = 7.577$ (2), $b = 10.510$ (2), $c = 35.399$ (7) Å, $V = 2819$ (1) Å^3, $Z = 4$, $D_x = 1.173$ g cm^{-3}, $\lambda(\text{Mo } K\alpha) = 0.71073$ Å, $\mu = 0.69$ cm^{-1}, $F(000) = 1096$, $T = 153$ K, $R = 0.0497$ for 2235 observed reflections. The compound investigated is found to be a (22*S*)-epimer.

Introduction. Steroids having a lanostane skeleton and oxygen function in their side chain at C22 exhibit some useful biological properties (Kamernitzky & Reshetova, 1977). Isolation of such compounds from natural products and their

synthesis may be of considerable interest. We have synthesized two isomers [(22*R*) and (11*S*)] of 3β-acetoxy-20-(3-isopropylisoxazolin-5-yl)-4,4,14α-trimethylpregn-8(9)-ene (1). Biological activity of such steroid derivatives depends on the configuration of the C22 centre. Therefore the determination of chirality at the C22 atom in one epimer is of primary importance especially taking into account that further transformations proceed without inversion at the C22 atom.
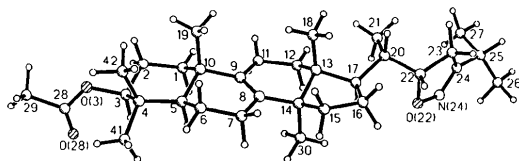
Experimental. The title compound (1) was prepared from 3β-acetoxy-25,26,27-trinorlanosta-8,22-diene (Poyser, Hirtzbach & Ourisson, 1974; Akhrem, Khripach, Litvinovskaya & Baranovsky, 1989) *via*

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Table 1. *Atomic coordinates* ($\times 10^4$) *and equivalent isotropic displacement coefficients* ($\text{Å}^2 \times 10^3$)

U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
C1	-4261 (6)	-8367 (5)	-1423 (1)	29 (1)
C2	-3941 (6)	-8145 (5)	-1001 (1)	33 (1)
C3	-2270 (6)	-8802 (4)	-875 (1)	30 (1)
C4	-602 (6)	-8423 (5)	-1092 (1)	32 (1)
C5	-1013 (5)	-8536 (4)	-1524 (1)	25 (1)
C6	563 (5)	-8180 (5)	-1770 (1)	33 (1)
C7	269 (5)	-8554 (4)	-2175 (1)	28 (1)
C8	-1607 (5)	-8453 (4)	-2315 (1)	20 (1)
C9	-2964 (5)	-8232 (4)	-2085 (1)	21 (1)
C10	-2737 (5)	-7883 (4)	-1667 (1)	22 (1)
C11	-4854 (5)	-8180 (4)	-2236 (1)	24 (1)
C12	-5133 (6)	-8417 (4)	-2662 (1)	26 (1)
C13	-3518 (5)	-8038 (4)	-2890 (1)	20 (1)
C14	-1910 (5)	-8785 (4)	-2723 (1)	21 (1)
C15	-446 (5)	-8440 (4)	-3008 (1)	28 (1)
C16	-1400 (5)	-8454 (5)	-3395 (1)	29 (1)
C17	-3431 (5)	-8446 (4)	-3313 (1)	23 (1)
C18	-3232 (6)	-6584 (4)	-2859 (1)	29 (1)
C19	-2675 (7)	-6409 (4)	-1655 (1)	33 (1)
C20	-4464 (6)	-7686 (4)	-3613 (1)	28 (1)
C21	-6452 (6)	-7632 (5)	-3531 (1)	33 (1)
C22	-4096 (6)	-8276 (4)	-4000 (1)	31 (1)
C23	-5102 (6)	-7703 (5)	-4336 (1)	36 (1)
C24	-6386 (6)	-8751 (4)	-4418 (1)	31 (1)
C25	-7878 (7)	-8668 (5)	-4700 (1)	36 (2)
C26	-8099 (7)	-9884 (5)	-4924 (2)	49 (2)
C27	-9581 (7)	-8324 (6)	-4490 (2)	50 (2)
C28	-2042 (6)	-9357 (4)	-215 (1)	33 (1)
C29	-1821 (7)	-8782 (5)	172 (1)	45 (2)
C30	-2141 (6)	-10244 (4)	-2741 (1)	30 (1)
C41	850 (7)	-9396 (6)	-991 (1)	48 (2)
C42	54 (7)	-7110 (5)	-977 (1)	42 (2)
O3	-2013 (4)	-8465 (3)	-478 (1)	35 (1)
O22	-4629 (4)	-9612 (3)	-3993 (1)	37 (1)
O28	-2253 (6)	-10468 (3)	-273 (1)	57 (1)
N24	-6110 (5)	-9778 (4)	-4240 (1)	36 (1)

Perspective view of compound (1).

Table 2. *Torsion angles* (°)

C10	C1	C2	C3	-58.8	C9	C8	C14	C15	152.8
C1	C2	C3	C4	56.5	C9	C8	C14	C30	-87.5
C1	C2	C3	O3	176.2	C12	C13	C14	C8	-60.8
C2	C3	C4	C5	-50.2	C12	C13	C14	C15	173.4
C2	C3	C4	C41	-167.0	C12	C13	C14	C30	59.5
C2	C3	C4	C42	74.9	C17	C13	C14	C8	174.9
O3	C3	C4	C5	-169.2	C17	C13	C14	C15	49.1
O3	C3	C4	C41	74.0	C17	C13	C14	C30	-64.8
O3	C3	C4	C42	-44.1	C18	C13	C14	C8	58.7
C3	C4	C5	C6	-180.0	C18	C13	C14	C15	-67.1
C3	C4	C5	C10	49.5	C18	C13	C14	C30	179.0
C41	C4	C5	C6	-63.8	C8	C14	C15	C16	-160.7
C41	C4	C5	C10	165.6	C13	C14	C15	C16	-39.1
C42	C4	C5	C6	55.8	C30	C14	C15	C16	79.6
C42	C4	C5	C10	-74.7	C14	C15	C16	C17	14.7
C4	C5	C6	C7	168.1	C12	C13	C17	C16	-155.8
C10	C5	C6	C7	-58.6	C12	C13	C17	C20	79.3
C5	C6	C7	C8	34.5	C14	C13	C17	C16	-39.4
C6	C7	C8	C9	-9.6	C14	C13	C17	C20	-164.3
C6	C7	C8	C14	178.2	C18	C13	C17	C16	77.9
C7	C8	C9	C10	8.5	C18	C13	C17	C20	-47.0
C7	C8	C9	C11	-178.0	C15	C16	C17	C13	15.7
C14	C8	C9	C10	-179.7	C15	C16	C17	C20	145.5
C14	C8	C9	C11	-6.1	C13	C17	C20	C21	-57.9
C2	C1	C10	C5	55.6	C13	C17	C20	C22	178.5
C2	C1	C10	C9	173.9	C16	C17	C20	C21	-178.3
C2	C1	C10	C19	-68.8	C16	C17	C20	C22	58.1
C4	C5	C10	C1	-52.8	C17	C20	C22	C23	176.2
C4	C5	C10	C9	-174.2	C17	C20	C22	O22	58.4
C4	C5	C10	C19	69.1	C21	C20	C22	C23	51.7
C6	C5	C10	C1	176.0	C21	C20	C22	O22	-66.1
C6	C5	C10	C9	54.6	C20	C22	C23	C24	-108.0
C6	C5	C10	C19	-62.1	O22	C22	C23	C24	12.2
C8	C9	C10	C1	-148.8	C22	C23	C24	C25	173.1
C8	C9	C10	C5	-30.5	C22	C23	C24	N24	-9.2
C8	C9	C10	C19	91.5	C23	C24	C25	C26	139.6
C11	C9	C10	C1	37.4	C23	C24	C25	C27	-96.9
C11	C9	C10	C5	155.6	N24	C24	C25	C26	-37.9
C11	C9	C10	C19	-82.4	N24	C24	C25	C27	85.5
C8	C9	C11	C12	1.2	C2	C3	O3	C28	116.9
C10	C9	C11	C12	175.1	C4	C3	O3	C28	-118.8
C9	C11	C12	C13	-27.8	C29	C28	O3	C3	-177.7
C11	C12	C13	C14	55.5	O28	C28	O3	C3	0.7
C11	C12	C13	C17	168.7	C20	C22	O22	N24	112.8
C11	C12	C13	C18	-65.0	C23	C22	O22	N24	-12.3
C7	C8	C14	C13	-151.1	C23	C24	N24	O22	1.9
C7	C8	C14	C15	-34.9	C25	C24	N24	O22	179.7
C7	C8	C14	C30	84.8	C22	O22	N24	C24	6.9
C9	C8	C14	C13	36.6					

1,3-dipolar cycloaddition of isopropylnitrile oxide. Suitable crystals of the individual epimer (m.p. 522–523 K) were prepared by crystallization from EtOAc.

The X-ray intensity data from a colourless $0.30 \times 0.35 \times 0.85$ mm crystal were collected with an automated Syntex $P2_1$ four-circle diffractometer at 153 K using graphite-monochromated Mo $K\alpha$ radiation. The unit-cell parameters were determined on the basis of accurately measured positions of 24 reflections in the $13 < \theta < 14°$ range. The intensities of 3733 reflections ($0 \le h \le 9$, $0 \le k \le 13$, $0 \le l \le 46$) were measured using $\theta/2\theta$ scans (background/peak time ratio 0.25) in the θ range from 2.0 to 30.0° with a variable scan speed ($3.0–30.0°$ min^{-1} in ω). The intensities of two standard reflections (measured every 98 reflections) did not show any significant changes [$\delta(I) < 3\%$].

All calculations were performed with an IBM-PC/AT computer using *SHELXTL-Plus* (PC Version; Sheldrick, 1989). The intensities of 2235 independent observed [$I > 3\sigma(I)$] reflections corrected for Lorentz and polarization factors were used. The structure was solved using direct methods and refined by full-matrix least squares in anisotropic approximation for non-H atoms. H atoms were placed in calculated positions and refined isotropically with a fixed $U_{iso} = 0.08$ Å^2. The final refinement of 289 parameters converged to $R = 0.0497$, $wR = 0.0498$ [$w^{-1} = \sigma^2(F) + 99.000F^2$], $S = 1.17$, mean $(\Delta/\sigma) = 0.170$, $0.23 > \Delta\rho > -0.19$ e Å^{-3}.

Discussion. Atomic coordinates and equivalent isotropic thermal parameters are given in Table 1.* The

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molecular structure with atom numbering is shown in Fig. 1. Bond lengths and angles are unexceptional (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987; Duax & Norton, 1975).

The determination of absolute configuration of the C22 chiral centre, which turned out to be *S*, was based on the known chirality of the steroid framework. The main torsion angles, which characterize the molecular conformation, are given in Table 2. The steroid framework conformation coincides with a standard for $\Delta^{8(9)}$-pregnanes (Duax & Norton, 1975), *viz.* a chair for the *A* ring, a 5α-sofa for the *B* ring, a 13β-sofa for the *C* ring and a 14α-envelope for the *D* ring. The orientation of the side chain at C17, characterized by the torsion angle C16 C17 C20 C21 = $-178\cdot3°$, may be considered as sterically least strained. The oxazoline ring is in fact planar. The orientation of the 3β-acetoxy group [with the carbonyl O and H(C3) atoms disposed close to each other] is similar to that usually observed in most of the analogous steroid derivatives (Duax & Norton, 1975).

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