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Levonorgestrel Cyclopentylcarboxylate 3-Oxime Dimethyl Sulfoxide Solvate

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Abstract. $C_{27}H_{38}NO_3.C_2H_6OS$, $M_r = 502{\cdot}73$, orthorhombic, $P2_12_12_1$, $a = 9{\cdot}619$ (5), $b = 10{\cdot}111$ (6), $c = 28{\cdot}33$ (1) Å, $V = 2755$ (4) Å^3, $Z = 4$, $D_x = 1{\cdot}212$ g cm^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, $\mu = 1{\cdot}44$ cm^{-1}, $F(000) = 1092$, $T = 190$ K, final $R = 0{\cdot}060$ for 1494 unique observed reflections [$I > 3.0\sigma(I)$], $wR = 0.070$.

Experimental. The title compound (Fig. 1) has been tested by the World Health Organization as a long-acting injectable steroid contraceptive. Crystallization experiments showed that this progestin exhibits two crystalline polymorphs, three closely related amorphous forms and one dimethyl sulfoxide solvate. There was also some question as to the configuration of the oxime with respect to the double bond in ring *A*. The structure of the solvate, reported here, was carried out as part of the structural characterization of the material.

Colorless single crystals were obtained by slow evaporation from dimethyl sulfoxide. A crystal of approximate dimensions 0.45 × 0.40 × 0.20 mm, m.p. 386 K, was used for data collection on an Enraf–Nonius CAD-4 diffractometer with monochromatic Mo $K\alpha$ radiation. Lattice parameters were obtained from a least-squares analysis of 25 reflections $30 < 2\theta < 34°$. Data were collected using an ω–2θ scan to $2\theta_{max} = 50.0°$, $h = -11$ to 11, $k = 0$ to 9, $l = 0$ to 27. Of the 5282 reflections which were measured, 2813 were unique ($R_{int} = 0.099$); equivalent reflections were merged. The intensities of three representative reflections (200, 020, 0,0,$\overline{12}$) measured after every 100 min of X-ray exposure time indicated crystal and electronic stability. An empirical absorption correction, using the program *DIFABS* (Walker & Stewart, 1983), was applied which resulted in transmission factors varying from 0.76 to 1.22. The data were corrected for Lorentz and polarization effects.

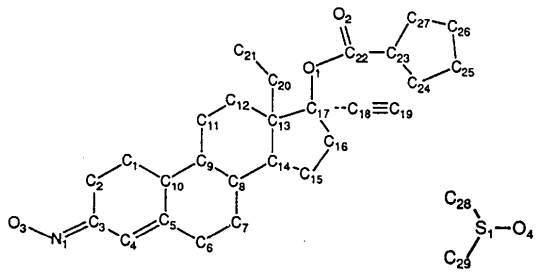

Fig. 1. Diagram of the molecule including atomic numbering.

The structure was solved by direct methods using *PHASE* (Calabrese, 1972). Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the structure factor calculation in idealized positions ($d_{C-H} = 0.95$ Å) and were assigned isotropic displacement parameters which were 20% greater than the B_{eq} value of the atom to which they were bonded. The final cycle of full-matrix least-squares refinement was based on 1494 observed reflections [$I > 3.0\sigma(I)$] and 316 variable parameters and converged (largest parameter shift was 0.54 times its e.s.d.) with unweighted and weighted agreement factors $R = 0.060$, $wR = 0.070$. The standard deviation of an observation of unit weight was $[(\sum w||F_o| - |F_c||)^2/(N_o - N_v)]^{1/2}$. The minimum and maximum peaks on the final difference Fourier map correspond to −0.42 and 0.26 e Å^{-3} respectively. Neutral-atom scattering factors were taken from Cromer & Waber (1974). All

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Table 1. *Positional parameters and B_{eq} values for the title compound*

$B_{eq} = (B_{11}B_{22}B_{33})^{1/3}$.

	x	y	z	B_{eq}(Å^2)
O1	1.6513 (5)	0.2448 (5)	0.8665 (2)	2.4 (2)
O2	1.6396 (7)	0.1727 (6)	0.9413 (2)	3.5 (3)
O3	0.8858 (8)	0.1933 (8)	0.5917 (2)	5.7 (4)
N1	0.840 (1)	0.2860 (8)	0.6180 (3)	6.3 (5)
C1	1.237 (1)	0.355 (1)	0.6422 (3)	3.4 (4)
C2	1.122 (1)	0.255 (1)	0.6340 (3)	4.6 (5)
C3	0.985 (1)	0.314 (1)	0.6407 (3)	5.2 (6)
C4	0.970 (1)	0.416 (1)	0.6753 (3)	4.5 (5)
C5	1.074 (1)	0.466 (1)	0.6989 (3)	3.2 (4)
C6	1.058 (1)	0.555 (1)	0.7405 (3)	3.5 (4)
C7	1.1136 (9)	0.4843 (9)	0.7845 (3)	2.9 (4)
C8	1.2647 (8)	0.4387 (8)	0.7771 (3)	2.0 (3)
C9	1.2777 (8)	0.3509 (8)	0.7332 (3)	2.1 (3)
C10	1.2247 (8)	0.4251 (8)	0.6892 (3)	2.3 (3)
C11	1.4283 (9)	0.3010 (8)	0.7266 (3)	2.4 (3)
C12	1.4837 (9)	0.2318 (7)	0.7703 (2)	2.2 (3)
C13	1.4757 (7)	0.3228 (7)	0.8127 (2)	1.7 (3)
C14	1.3248 (8)	0.3668 (9)	0.8200 (2)	2.1 (3)
C15	1.326 (1)	0.438 (1)	0.8676 (3)	3.3 (4)
C16	1.433 (1)	0.3570 (9)	0.8966 (3)	2.7 (4)
C17	1.5013 (8)	0.2580 (6)	0.8614 (2)	1.6 (3)
C18	1.5720 (9)	0.4423 (8)	0.8077 (3)	2.3 (3)
C19	1.7132 (9)	0.420 (1)	0.7852 (3)	3.1 (4)
C20	1.4377 (9)	0.1250 (8)	0.8654 (2)	2.2 (3)
C21	1.381 (1)	0.0228 (9)	0.8686 (3)	2.8 (4)
C22	1.7065 (9)	0.204 (1)	0.9078 (3)	2.8 (4)
C23	1.862 (1)	0.208 (1)	0.9038 (3)	3.0 (4)
C24	1.939 (1)	0.124 (1)	0.9412 (3)	4.3 (5)
C25	2.070 (1)	0.208 (1)	0.9505 (4)	4.7 (5)
C26	2.019 (1)	0.347 (1)	0.9511 (3)	5.0 (5)
C27	1.914 (1)	0.355 (1)	0.9122 (3)	4.1 (5)
S1	0.4940 (3)	0.2133 (3)	0.55069 (8)	4.2 (1)
O4	0.6396 (7)	0.1776 (7)	0.5374 (2)	4.4 (3)
C28	0.459 (1)	0.367 (1)	0.5248 (4)	5.8 (6)
C29	0.386 (1)	0.119 (1)	0.5126 (3)	4.5 (5)

calculations were performed using the *TEXSAN* crystallographic software package of the Molecular Structure Corporation (1985).

Atomic positions are listed in Table 1; bond distances and angles are presented in Table 2.* The *PLUTO* (Motherwell & Clegg, 1978) stereo drawing of the molecule is given in Fig. 2. The molecule crystallizes as a solvate with one molecule of solvent per molecule of steroid. The torsion angle O3—N1—C3—C4 is $-177.7°$, so the conformation of the *N*-oxime group is clearly *anti* to the C3—C4 bond in ring *A*. In solution, there is considerable lability of this group and an equilibrium mixture of *syn* and *anti* isomers is obtained. There is no evidence from the refinement (*i.e.* temperature factors or residual electron density) for any presence of the *cis* isomer in the crystal. The process of crystallization thus leads preferentially to the *anti* isomer.

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* Lists of structure factors, anisotropic thermal parameters, H-atom parameters, torsion angles and bond lengths and angles involving H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54521 (27 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Bond lengths* (Å) *and bond angles* (°) *for the title compound*

O1—C22	1.350 (9)	C12—C13	1.52 (1)
O1—C17	1.46 (1)	C13—C18	1.53 (1)
O2—C22	1.19 (1)	C13—C14	1.53 (1)
O3—N1	1.28 (1)	C13—C17	1.55 (1)
N1—C3	1.56 (1)	C14—C15	1.53 (1)
C1—C2	1.51 (1)	C15—C16	1.55 (1)
C1—C10	1.52 (1)	C16—C17	1.56 (1)
C2—C3	1.46 (2)	C17—C20	1.48 (1)
C3—C4	1.43 (2)	C18—C19	1.52 (1)
C4—C5	1.31 (1)	C20—C21	1.17 (1)
C5—C6	1.49 (1)	C22—C23	1.50 (1)
C5—C10	1.53 (1)	C23—C24	1.55 (1)
C6—C7	1.53 (1)	C23—C27	1.58 (1)
C7—C8	1.54 (1)	C24—C25	1.54 (1)
C8—C14	1.53 (1)	C25—C26	1.50 (1)
C8—C9	1.53 (1)	C26—C27	1.50 (1)
C9—C10	1.54 (1)	S1—O4	1.494 (7)
C9—C11	1.55 (1)	S1—C28	1.75 (1)
C11—C12	1.52 (1)	S1—C29	1.78 (1)

C22—O1—C17	120.3 (6)	C18—C13—C17	108.8 (6)
O3—N1—C3	94 (1)	C14—C13—C17	98.8 (6)
C2—C1—C10	113.2 (8)	C15—C14—C8	118.6 (7)
C3—C2—C1	111.2 (9)	C15—C14—C13	104.4 (6)
C4—C3—C2	118.9 (9)	C8—C14—C13	112.8 (6)
C4—C3—N1	109 (1)	C14—C15—C16	102.8 (7)
C2—C3—N1	132 (1)	C15—C16—C17	106.4 (6)
C5—C4—C3	123 (1)	O1—C17—C20	108.6 (6)
C4—C5—C6	123.8 (8)	O1—C17—C13	106.6 (6)
C4—C5—C10	122.0 (9)	O1—C17—C16	114.5 (6)
C6—C5—C10	113.8 (7)	C20—C17—C13	112.8 (6)
C5—C6—C7	108.9 (7)	C20—C17—C16	111.0 (6)
C6—C7—C8	111.0 (6)	C13—C17—C16	103.3 (6)
C14—C8—C9	109.8 (6)	C19—C18—C13	117.7 (7)
C14—C8—C7	112.9 (6)	C21—C20—C17	176.9 (9)
C9—C8—C7	111.2 (7)	O2—C22—O1	124.0 (8)
C8—C9—C10	110.3 (6)	O2—C22—C23	127.5 (8)
C8—C9—C11	111.3 (6)	O1—C22—C23	108.5 (7)
C10—C9—C11	111.8 (6)	C22—C23—C24	114.2 (8)
C1—C10—C5	110.8 (7)	C22—C23—C27	109.3 (8)
C1—C10—C9	117.2 (7)	C24—C23—C27	105.1 (7)
C5—C10—C9	107.4 (6)	C25—C24—C23	102.1 (8)
C12—C11—C9	112.4 (6)	C26—C25—C24	104.2 (8)
C13—C12—C11	110.4 (6)	C27—C26—C25	105.3 (8)
C12—C13—C18	112.0 (6)	C26—C27—C23	106.0 (8)
C12—C13—C14	109.3 (6)	O4—S1—C28	106.8 (5)
C12—C13—C17	116.2 (6)	O4—S1—C29	105.4 (4)
C18—C13—C14	110.9 (6)	C28—S1—C29	96.3 (5)

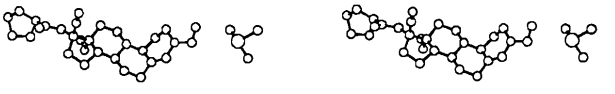

Fig. 2. Stereo drawing of the molecule, including the dimethyl sulfoxide of crystallization.

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