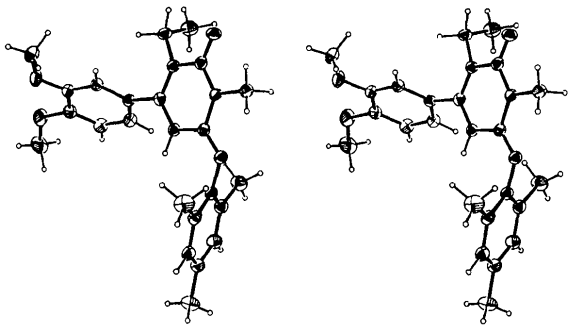

Fig. 1. Stereographic view of the molecular conformation of FK664 (*ORTEP*II).

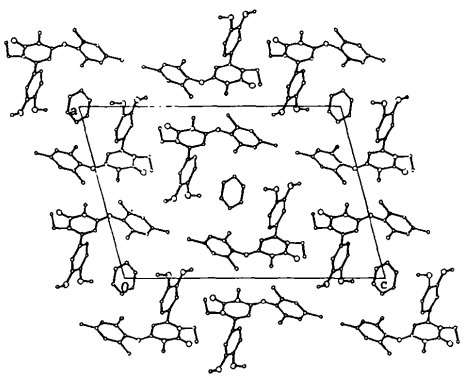

Fig. 2. Crystal packing diagram of FK664 along the *b* axis (*PLUTO*).

the phenyl ring *C* probably keeps away from the bulky N(1) ethyl group. Thus, FK664 takes a crystallographically and/or energetically reasonable conformation in three planes, *A*, *B* and *C*. Fig. 2 shows a packing diagram of FK664 benzene solvate. The crystal solvents, benzene molecules, are located at inversion centers in the crystal lattice. Because there are neither inter- nor intramolecular hydrogen bonds in the FK664 benzene solvate crystal, the packing force should be due to van der Waals forces only.

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Structure of an Analogue of the Steroidal Isoxazole Danazol, Ethyl 17α-Ethynyl-17-hydroxy-4-androsteno[2,3-*d*]isoxazole-3′-carboxylate*

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Abstract. $C_{25}H_{31}NO_4$, $M_r = 409{\cdot}5$, orthorhombic, $P2_12_12_1$, $a = 7{\cdot}428\ (2)$, $b = 11{\cdot}391\ (1)$, $c = 26{\cdot}677\ (3)$ Å, $V = 2257\ (1)$ Å^3, $Z = 4$, $D_x = 1{\cdot}205$ g cm^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 6{\cdot}135$ cm^{-1}, $F(000) = 880$, ambient temperature, $R = 0{\cdot}043$ for 1277 unique reflections with $I > 2\sigma(I)$. The heterocyclic ring is planar. The *B*/*C* and *C*/*D* ring fusions are *trans*. Ring *A* has a flattened sofa conformation. The acetylenic group is axial (α) and is on the opposite face of the molecule to the methyl groups. Intermolecular O(hydroxy)···O(isoxazole) hydrogen bonds [2·871 (4) Å] exist in the crystal structure.

* IUPAC name: ethyl 1-ethynyl-1-hydroxy-10a,12a-dimethyl-2,3,3a,3b,4,5,10,10a,10b,11,12,12a-dodecahydro-1*H*-cyclopenta-[7,8]phenanthro[3,2-*d*]isoxazole-9-carboxylate.

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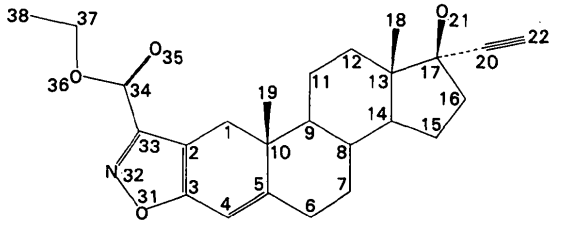
Introduction. Danazol, a steroidal isoxazole with interesting pharmacological properties, is being increasingly used for the treatment of a wide range of hormonal and endocrinological disorders (Reyniak & Lauersen, 1982; Madanes & Farber, 1982).

The drug is rapidly and extensively metabolized *in vivo* by an initial cleavage of the heterocyclic ring (Rosi, Neumann, Christiansen, Schane & Potts, 1977; Davison, Banks & Fritz, 1976). The parent drug is reported to be the pharmacologically active entity and therefore metabolism of the heterocyclic ring can be considered adverse (Potts, 1977). The title compound (I) was synthesized as part of a structure–activity study with the objective of blocking or retarding metabolism of the heterocyclic ring. In the title compound an ethoxycarbonyl group replaces the H atom of danazol at C33. The synthesis, biological activity and metabolism of the compound are described elsewhere (Nicholls, 1986).



(I)

Experimental. Crystals are white and lath-shaped, elongated along **a**. The crystal selected for data collection was of size 0·75 × 0·15 × 0·10 mm. Preliminary unit-cell dimensions and space-group information were obtained from Weissenberg photographs. Accurate cell parameters were obtained by least-squares refinement of the θ values of 25 reflections with $10 < \theta < 35°$ measured on an Enraf–Nonius CAD-4 diffractometer. Intensity data were collected to a maximum $(\sin\theta)/\lambda$ value of 0·562 Å^{-1} using Ni-filtered Cu $K\alpha$ radiation and an ω–2θ scan technique. A total of 2304 measurements were made for reflections with $0 \le h \le 8$, $0 \le k \le 12$, $0 \le l \le 29$. Three reference reflections were measured after every 60 min of X-ray exposure time; the overall variation in the sum of their intensities was 5%. The final data set consisted of 1952 unique reflections, of which 675 had $I < 2\sigma(I)$ and were thereby designated unobserved.

The structure was solved by direct methods (Main *et al.*, 1982). Full-matrix least-squares refinement of the scale factor and positional and anisotropic thermal parameters for all non-H atoms was carried out using the Enraf–Nonius *SDP* (B. A. Frenz & Associates Inc., 1983). Weights were assigned as $w = 1/\sigma^2(F_o)$ and the quantity minimized was $\sum w(F_o - F_c)^2$. H atoms were located from a difference Fourier synthesis but subsequently fixed in calculated positions with idealized geometry, assuming C–H and O–H distances of 1·0 and 0·95 Å respectively. Each H atom was assigned a fixed isotropic thermal parameter $B_{iso} = 5{\cdot}0$ Å^2. Refinement converged to give final residuals $R = 0{\cdot}043$ and $wR = 0{\cdot}046$. The maximum Δ/σ value in the final cycle of refinement was 0·01; the maximum variations in the final difference Fourier map were within $\pm 0{\cdot}16$ e Å^{-3}. Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974). All computations were performed on a VAX 11/750 computer.

Table 1. *Non-H-atom positional and equivalent isotropic thermal parameters, with e.s.d.'s in parentheses*

$B_{eq} = \frac{8}{3}\pi^2 \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i . \mathbf{a}_j$.

	x	y	z	B_{eq}(Å^2)
C1	0·8107 (6)	0·6386 (4)	0·1000 (2)	3·0 (1)
C2	0·7527 (6)	0·5874 (4)	0·0503 (1)	2·77 (9)
C3	0·5847 (6)	0·6044 (4)	0·0341 (2)	3·4 (1)
C4	0·4501 (6)	0·6738 (4)	0·0582 (2)	3·5 (1)
C5	0·5005 (6)	0·7404 (4)	0·0970 (2)	2·74 (9)
C6	0·3686 (7)	0·8228 (5)	0·1210 (2)	4·1 (1)
C7	0·3861 (6)	0·8288 (4)	0·1782 (2)	3·5 (1)
C8	0·5787 (6)	0·8555 (4)	0·1933 (1)	2·64 (9)
C9	0·7058 (6)	0·7619 (4)	0·1721 (1)	2·40 (9)
C10	0·6976 (6)	0·7493 (4)	0·1143 (2)	2·39 (9)
C11	0·9021 (6)	0·7771 (4)	0·1907 (2)	3·0 (1)
C12	0·9141 (6)	0·7887 (4)	0·2484 (2)	3·2 (1)
C13	0·7914 (6)	0·8863 (4)	0·2673 (1)	2·6 (1)
C14	0·6006 (6)	0·8591 (4)	0·2504 (2)	2·90 (9)
C15	0·4815 (7)	0·9447 (4)	0·2801 (2)	4·2 (1)
C16	0·5846 (8)	0·9591 (5)	0·3301 (2)	4·6 (1)
C17	0·7639 (7)	0·8938 (4)	0·3248 (2)	3·3 (1)
C18	0·8601 (7)	1·0059 (4)	0·2486 (2)	4·1 (1)
C19	0·7759 (7)	0·8559 (4)	0·0864 (2)	3·9 (1)
C20	0·7566 (7)	0·7769 (4)	0·3492 (2)	3·9 (1)
O21	0·9120 (5)	0·9572 (3)	0·3466 (1)	5·00 (8)
C22	0·7485 (9)	0·6900 (5)	0·3722 (2)	5·7 (1)
O31	0·5568 (5)	0·5449 (3)	−0·0095 (1)	4·70 (8)
N32	0·7168 (5)	0·4856 (3)	−0·0220 (1)	4·29 (9)
C33	0·8315 (6)	0·5126 (4)	0·0140 (2)	3·0 (1)
C34	1·0134 (6)	0·4612 (4)	0·0140 (2)	3·3 (1)
O35	1·1211 (4)	0·4792 (3)	0·0466 (1)	4·77 (8)
O36	1·0428 (5)	0·3926 (3)	−0·0253 (1)	4·43 (8)
C37	1·2156 (8)	0·3325 (5)	−0·0275 (2)	4·43 (8)
C38	1·2292 (9)	0·2727 (6)	−0·0754 (2)	8·0 (2)

Discussion. Atomic coordinates and equivalent isotropic thermal parameters for non-H atoms are given in Table 1* and Table 2 contains intramolecular bond lengths and angles. Fig. 1 shows two orthogonal perspective views of the molecular structure.

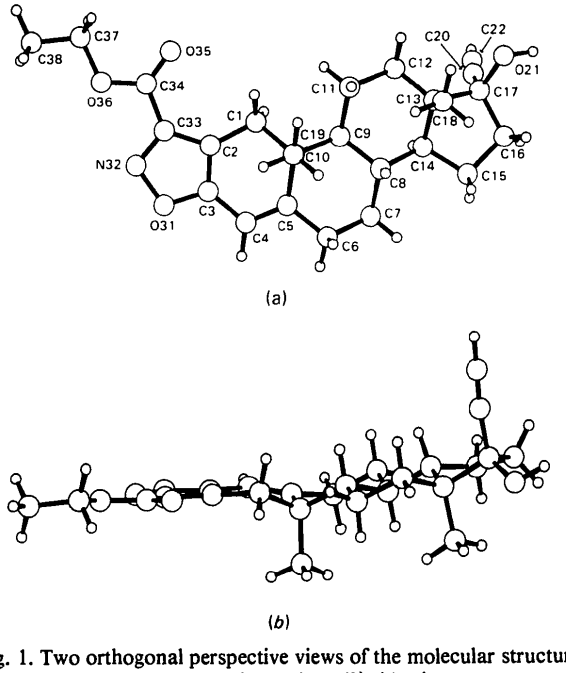
The heterocyclic ring is planar within experimental error; atoms C4, C34, O35 and O36 lie close to the least-squares plane defined by the five ring atoms at distances from it of 0·011 (5), 0·053 (4), 0·099 (3) and 0·063 (3) Å respectively. The values of the N32–C33–C34–O35 and C2–C33–C34–O36 torsion

* Lists of structure factors, anisotropic thermal parameters for non-H atoms and calculated H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51030 (27 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 2. *Intramolecular bond lengths* (Å) *and angles* (°)

C1–C2	1·512 (6)	C12–C13	1·524 (6)
C1–C10	1·562 (6)	C13–C14	1·519 (6)
C2–C3	1·334 (7)	C13–C17	1·550 (6)
C2–C33	1·415 (6)	C13–C18	1·538 (6)
C3–C4	1·428 (7)	C14–C15	1·538 (7)
C3–O31	1·361 (5)	C15–C16	1·547 (7)
C4–C5	1·337 (6)	C16–C17	1·532 (7)
C5–C6	1·500 (7)	C17–C20	1·484 (7)
C5–C10	1·539 (6)	C17–O21	1·438 (6)
C6–C7	1·534 (6)	C20–C22	1·166 (7)
C7–C8	1·517 (6)	O31–N32	1·406 (5)
C8–C9	1·533 (6)	N32–C33	1·321 (6)
C8–C14	1·531 (6)	C33–C34	1·472 (7)
C9–C10	1·549 (6)	C34–O35	1·200 (5)
C9–C11	1·550 (6)	C34–O36	1·326 (5)
C10–C19	1·539 (6)	O36–C37	1·456 (7)
C11–C12	1·547 (6)	C37–C38	1·452 (8)

C2–C1–C10	111·9 (4)	C12–C13–C17	116·6 (4)
C1–C2–C3	119·6 (4)	C12–C13–C18	109·8 (4)
C1–C2–C33	135·5 (4)	C14–C13–C17	100·5 (3)
C3–C2–C33	104·7 (4)	C14–C13–C18	113·2 (4)
C2–C3–C4	126·1 (4)	C17–C13–C18	108·5 (3)
C2–C3–O31	110·3 (4)	C8–C14–C13	113·6 (4)
C4–C3–O31	123·6 (4)	C8–C14–C15	118·0 (4)
C3–C4–C5	117·9 (4)	C13–C14–C15	104·7 (4)
C4–C5–C6	120·2 (4)	C14–C15–C16	103·2 (4)
C4–C5–C10	122·4 (4)	C15–C16–C17	107·4 (4)
C6–C5–C10	116·9 (4)	C13–C17–C16	103·5 (4)
C5–C6–C7	113·4 (4)	C13–C17–C20	112·9 (4)
C6–C7–C8	110·7 (4)	C13–C17–O21	109·1 (4)
C7–C8–C9	110·1 (3)	C16–C17–C20	111·3 (4)
C7–C8–C14	111·7 (4)	C16–C17–O21	112·6 (4)
C9–C8–C14	108·7 (3)	C20–C17–O21	107·5 (4)
C8–C9–C10	114·1 (3)	C17–C20–C22	174·2 (5)
C8–C9–C11	112·5 (3)	C3–O31–N32	108·2 (3)
C10–C9–C11	111·5 (3)	O31–N32–C33	105·1 (3)
C1–C10–C5	112·7 (3)	C2–C33–N32	111·7 (4)
C1–C10–C9	107·3 (3)	C2–C33–C34	128·3 (4)
C1–C10–C19	108·4 (3)	N32–C33–C34	119·9 (4)
C5–C10–C9	110·0 (3)	C33–C34–O35	112·9 (4)
C5–C10–C19	105·5 (3)	C33–C34–O36	112·8 (4)
C9–C10–C19	113·1 (3)	O35–C34–O36	124·4 (4)
C9–C11–C12	112·5 (3)	C34–O36–C37	116·9 (4)
C11–C12–C13	110·9 (4)	O36–C37–C38	108·4 (5)
C12–C13–C14	108·1 (3)		



(a)

(b)

Fig. 1. Two orthogonal perspective views of the molecular structure of danazol: (*a*) top view; (*b*) side view.

Table 3. *Ring torsion angles* (°)

	Structure 1	Structure 2	This structure
Ring *A*			
C2–C1–C10–C5	45·5	42·5	55·1
C10–C1–C2–C3	−51·0	−55·4	−26·0
C1–C2–C3–C4	25·7	35·8	3·6
C2–C3–C4–C5	3·5	−5·2	9·2
C3–C4–C5–C10	−8·1	−8·1	3·3
C4–C5–C10–C1	−16·6	−11·7	−25·5
Ring *B*			
C6–C5–C10–C9	46·7	53·0	43·2
C10–C5–C6–C7	−48·0	−60·2	−46·7
C5–C6–C7–C8	52·8	58·6	52·9
C6–C7–C8–C9	−57·8	−54·2	−57·8
C7–C8–C9–C10	58·8	50·8	57·5
C8–C9–C10–C5	−51·8	−49·0	−48·4
Ring *C*			
C14–C8–C9–C11	−50·0	−55·9	−51·5
C8–C9–C11–C12	50·7	59·6	50·9
C9–C11–C12–C13	−54·1	−58·7	−53·6
C11–C12–C13–C14	55·9	49·8	57·4
C12–C13–C14–C8	−60·7	−47·4	−62·0
C9–C8–C14–C13	57·7	53·2	58·7
Ring *D*			
C17–C13–C14–C15	45·9	−38·8	45·4
C13–C14–C15–C16	−34·1	23·7	−32·2
C14–C15–C16–C17	8·9	0·7	6·0
C15–C16–C17–C13	18·9	−25·1	21·4
C14–C13–C17–C16	−39·2	39·4	−40·5

Structure 1: cholest-4-en-3-one (Sheldrick *et al.*, 1976). Structure 2: 20-methyl-14β,17α-pregn-4-en-3-one (Sheldrick, 1977). E.s.d.'s were not given for either structure. Average torsion-angle e.s.d. for the present structure is 0·6°.

angles are −177·3 (4) and 178·6 (4)° and the C33–C34 bond length is 1·472 (7) Å. These features, together with the lengths of the relevant endocyclic bonds, indicate delocalization of electron density both within the ring and extending into the C4–C5 and C34–O35–O36 regions. However, the C4–C5 and C2–C3 bond lengths [1·337 (6) and 1·334 (7) Å] show that these bonds have significantly more double-bond character than C2–C33 [1·415 (6) Å] and C3–C4 [1·428 (6) Å], indicating that the canonical form (I) is correct.

The steroid *A* ring (C1, C2, C3, C4, C5, C10) is in the envelope-like 'sofa' conformation, with C1 displaced by 0·414 (4) Å from the plane defined by the remaining atoms. It is flattened compared to the *A*-ring conformations found in analogous steroids (Table 3) on account of its fusion to the planar isoxazole ring. The *B* and *C* rings both adopt chair conformations in a manner similar to that found in other steroid derivatives with the 4-en-3-one feature, for example, in cholest-4-en-3-one (Sheldrick, Oeser, Caira, Nassimbeni & Pauptit, 1976) and 20-methyl-14β,17α-pregn-4-en-3-one (Sheldrick, 1977) (Table 3). The detailed *B*-, *C*- and *D*-ring conformations in the present structure match those in cholest-4-en-3-one to a high degree, rather than those in 20-methyl-14β,17α-pregn-4-en-3-one, on account of the *cis C/D* ring fusion in the latter structure. The *B/C* and *C/D* ring fusions here are both *trans*. The *D*-ring conformation is mid-way between those of ideal envelope and half-chair forms with a pseudorotation

phase angle of 46 (1)° (Altona, Geise & Romers, 1968). The molecule has an overall planar shape (Fig. 1*b*), with the acetylene group at C17 attached in an α (axial) position and the two methyl groups on the β face. The hydroxyl group is near-equatorial and the side chain attached at C33 is in an extended conformation.

In the crystal structure, the molecules are arranged in an end-to-end manner, with intermolecular hydrogen bonds between O21 and O31 [O···O distance is 2·871 (4) Å].

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Acta Cryst. (1988). C**44**, 1624–1627

Structure of (*R*)-1-[(*R*)-1-Phenylethylamino]benzylphosphonic Acid Sesquihydrate

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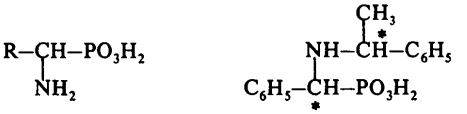
Abstract. $C_{15}H_{18}NO_3P.1{\cdot}5H_2O$, $M_r = 318{\cdot}35$, orthorhombic, $P2_12_12_1$, $a = 6{\cdot}587\ (2)$, $b = 11{\cdot}769\ (3)$, $c = 20{\cdot}575\ (5)$ Å, $V = 1595{\cdot}0$ Å^3, $Z = 4$, $D_m = 1{\cdot}326\ (1)$, $D_x = 1{\cdot}325$ Mg m^{-3}, $T = 291$ K, Mo $K\alpha$, $\lambda = 0{\cdot}71069$ Å, $\mu = 0{\cdot}20$ mm^{-1}, $F(000) = 676$, $R = 0{\cdot}043$ for 1797 reflexions. The molecule exists as a zwitterion: the amino group is protonated and the phosphonic acid group is ionized. The conformation of the molecule is *trans–gauche*, angles χ^1[P–C(1)–N–C(2)] and χ^2[C(1)–N–C(2)–C(phenyl)] being 169·6 (3) and 54·5 (4)°, respectively. The crystal structure is stabilized by three intermolecular hydrogen bonds and four van der Waals contacts. The absolute configuration of the molecule was assigned as *R,R* and is consistent with the known *R* configuration of (+)-1-phenylethylamine.

Introduction. The determination of the molecular structure and absolute configuration of 1-aminophosphonic acids (1) is of considerable importance in view of the established inhibition of enzymes involved in the metabolism of amino acids by the phosphonic acid analogues of substrates (Neuzil & Cassaigne, 1980; Brand & Lowenstein, 1978; Lejczak, Starzemska & Mastalerz, 1981).



(1)

(2)

Recently, we reported the synthesis and absolute configuration of (*S*)-2-methyl-1-[(*R*)-1-phenylethylamino]-1-propanephosphonic acid monohydrate (Sawka-Dobrowolska, Głowiak, Kowalik & Mastalerz, 1985) and (*R*)-1-[(*S*)-1-phenylethylamino]benzylphosphonic acid monohydrate (Głowiak, Sawka-Dobrowolska, Kowalik, Mastalerz, Soroka & Zoń, 1977). The (*R,S*) diastereoisomer of (2) was prepared by addition of diethylphosphite to the aldimine prepared from benzaldehyde and (–)-(*S*)-1-phenylethylamine.

In continuation of our studies on the crystal structure and configuration of optically active 1-aminophosphonic acids we now report X-ray results for the title compound (2).

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