

## 17 $\beta$ -Hydroxymethyl-1,3,5(10)-estratrien-3-ol Monohydrate

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**Abstract.** C<sub>19</sub>H<sub>26</sub>O<sub>2</sub>·H<sub>2</sub>O, monoclinic,  $P2_1$ ,  $a = 16.828$  (8),  $b = 13.664$  (7),  $c = 7.278$  (4) Å,  $\beta = 90.00$  (5)°,  $Z = 4$ ,  $d_c = 1.21$  Mg m<sup>-3</sup>. The structure, solved by direct methods, consists of sheets of molecules linked by hydrogen bonds to a molecule of water and lying parallel to the  $bc$  plane. The two independent molecules occur in different sheets.

**Introduction.** Diethylstilbestrol (DES) and estradiol have the same affinity for the estrogenic receptor and show the same biological activity. When we compare the crystalline conformations of the two molecules (Busetta & Hospital, 1972; Busetta, Courseille & Hospital, 1973) one of the most important differences observed is the distance between the two O atoms (10.9 Å for estradiol and 12.1 Å for DES). If one takes into account the molecule of water always present in the surroundings of the  $D$  ring of estradiol, this distance [between O(3) and the water] becomes 12.2 Å. In these conditions it is possible to propose that the real hormone could be the estradiol–water complex. To check this hypothesis, 17 $\beta$ -hydroxymethyl-1,3,5(10)-estratrien-3-ol was synthesized and the crystal structure analysis undertaken.

The crystals were grown by slow evaporation of a (1:1) methanol–water solution. The crystal used for data collection was prismatic with approximate dimensions 0.5 × 0.2 × 0.2 mm. Cell parameters and intensity data were obtained on a Siemens diffractometer using Cu  $K\alpha$  radiation ( $\lambda = 1.5418$  Å). The unit-cell parameters were determined from 16 reflexions ( $20^\circ < 2\theta < 42^\circ$ ) by a least-squares refinement. Intensities were collected for 2821 independent reflexions ( $\theta < 70^\circ$ ). A check reflexion was measured every fifty reflexions. Absorption corrections were not necessary. The structure was solved by direct methods with the program *SIR* (Giacovazzo, 1977; Busetta, 1978).

Atomic scattering factors were taken from *International Tables for X-ray Crystallography* (1974) for non-hydrogen atoms and from Stewart, Davidson & Simpson (1965) for H atoms. A block-diagonal

Table 1. Fractional coordinates ( $\times 10^4$ ) and equivalent isotropic thermal parameters for the non-hydrogen atoms

	$x$	$y$	$z$	$B_{eq}$ (Å <sup>2</sup> )
C(1)	1402 (4)	9858 (5)	-2167 (8)	3.8
C(2)	1576 (4)	10829 (5)	-2417 (9)	4.8
C(3)	1467 (3)	11480 (5)	-1023 (8)	3.4
C(4)	1167 (4)	11154 (5)	677 (8)	4.8
C(5)	984 (3)	10164 (4)	888 (8)	2.8
C(6)	651 (4)	9857 (5)	2770 (9)	5.0
C(7)	351 (4)	8795 (5)	2816 (9)	3.7
C(8)	929 (3)	8132 (5)	1816 (8)	3.4
C(9)	923 (3)	8418 (4)	-265 (7)	3.4
C(10)	1112 (3)	9499 (5)	-506 (7)	3.4
C(11)	1469 (4)	7741 (5)	-1385 (8)	4.5
C(12)	1303 (4)	6651 (5)	-1054 (8)	5.1
C(13)	1352 (3)	6402 (4)	996 (8)	3.2
C(14)	745 (3)	7044 (5)	1995 (8)	3.4
C(15)	691 (4)	6591 (5)	3907 (9)	4.4
C(16)	821 (5)	5456 (5)	3595 (10)	4.3
C(17)	1048 (3)	5373 (4)	1508 (8)	3.5
C(18)	2212 (3)	6559 (5)	1743 (11)	4.1
O(23)	1664 (3)	12458 (3)	-1274 (6)	4.8
C(27)	1624 (4)	4540 (5)	1114 (9)	3.4
O(37)	1250 (3)	3599 (3)	1447 (6)	4.8
C(51)	4303 (3)	5867 (5)	2409 (8)	3.7
C(52)	4113 (3)	4875 (5)	2545 (8)	3.9
C(53)	3754 (3)	4540 (5)	4162 (8)	3.9
C(54)	3589 (3)	5190 (4)	5562 (8)	4.4
C(55)	3785 (3)	6182 (5)	5427 (8)	3.2
C(56)	3575 (4)	6831 (5)	7009 (8)	4.8
C(57)	3874 (4)	7895 (5)	6843 (8)	3.7
C(58)	3790 (3)	8242 (4)	4863 (8)	3.7
C(59)	4341 (3)	7634 (4)	3620 (8)	3.4
C(60)	4147 (3)	6536 (4)	3830 (7)	3.0
C(61)	4336 (4)	7983 (5)	1629 (8)	3.3
C(62)	4461 (4)	9098 (5)	1454 (8)	3.9
C(63)	3868 (3)	9685 (4)	2659 (8)	3.4
C(64)	3960 (3)	9323 (4)	4643 (7)	3.2
C(65)	3515 (4)	10076 (5)	5752 (10)	4.1
C(66)	3630 (4)	11061 (5)	4737 (10)	4.7
C(67)	4031 (4)	10788 (5)	2861 (8)	3.7
C(68)	3016 (4)	9530 (6)	1912 (10)	4.6
O(73)	3552 (3)	3559 (3)	4401 (6)	4.7
C(77)	3766 (4)	11413 (5)	1289 (10)	4.4
O(87)	3998 (3)	12427 (3)	1550 (6)	4.3
O(90)	1843 (4)	3060 (5)	4813 (8)	8.0
O(91)	3319 (3)	3111 (4)	8364 (7)	6.4

least-squares refinement gave a final residual index of 0.051.\*

The weighting scheme used was  $\sqrt{w} = 1$  if  $|F_o| < p$  and  $\sqrt{w} = p/F_o$  if  $|F_o| > p$  with  $p = [F_{o(\max)}^2/10]^{1/2}$ . Table 1 gives the atomic coordinates of the structure.

**Discussion.** Bond lengths, and valence and dihedral angles of the two independent molecules are given in Fig. 1. Fig. 2, projections of both molecules on to the plane C(13)–C(17)–C(18), shows that their general conformations are very similar with no significant differences. Both conformations are close to those of estradiol (Busetta & Hospital, 1972; Busetta, Courseille, Geoffre & Hospital, 1972). The pentagonal *D* rings, defined by their  $\Delta$  and  $\varphi_m$  parameters (Altona, Geise & Romers, 1968), have a conformation midway between the theoretical  $\beta$  envelope and the theoretical half chair:  $\Delta = 18^\circ$ ,  $\varphi_m = 48^\circ$  for molecule (I);  $\Delta = 11^\circ$ ,  $\varphi_m = 44^\circ$  for molecule (II). The change of the usual 17 $\beta$  OH function to a 17 $\beta$  CH<sub>2</sub>OH function does not seem to affect the conformation of the pentagonal *D* ring in any particular way. Interactions between the H atoms on C(27) and the methyl group C(18) ensure that the hydroxyl function lies along the major axis of

\* Lists of structure factors and anisotropic thermal parameters, and the coordinates of the hydrogen atoms have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34960 (22 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

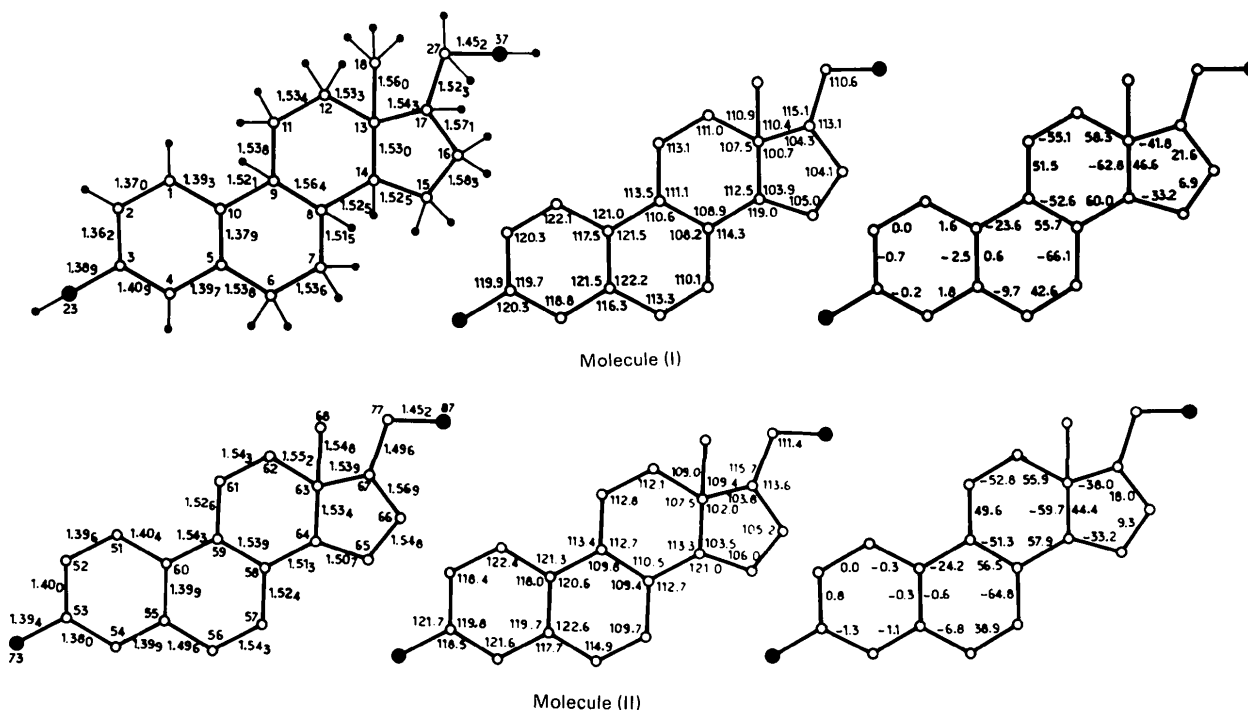


Fig. 1. Bond distances (Å), bond angles (°) and dihedral angles (°) for molecules (I) and (II) ( $\bar{\sigma} = 0.008$  Å,  $0.4^\circ$  and  $0.9^\circ$  respectively).

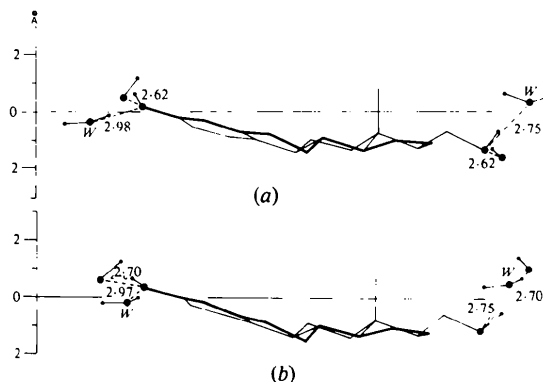
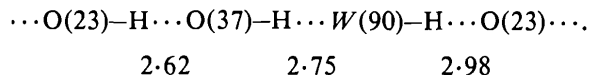


Fig. 2. Projections of (a) molecule (I) and (b) molecule (II) and their hydrogen bonds on the plane C(13)–C(17)–C(18).

the molecule. The distances between the two terminal O atoms are 12.28 Å and 12.32 Å for molecules (I) and (II). This result and the good value of the affinity coefficient for the receptor (Raynaud, Ojasoo, Bouton & Philibert, 1979) seem to confirm the hypothesis concerning the role played by the water in the estrogenic activity of estradiol.

The molecular arrangement and hydrogen bonding are interesting. The (001) projection (Fig. 3) shows sheets of molecules parallel to the *bc* plane. Each sheet is formed by identical molecules, so that in the *a* direction we find an alternating sequence of sheets of molecules (I) and (II). In one sheet, the crystal cohesion is mainly ensured in the *c* direction by a helicoidal

succession of hydrogen bonds involving a molecule of water. For the sheet of molecules (I) hydrogen-bond lengths ( $\text{\AA}$ ) are:



For the sheet of molecules (II) the values are:

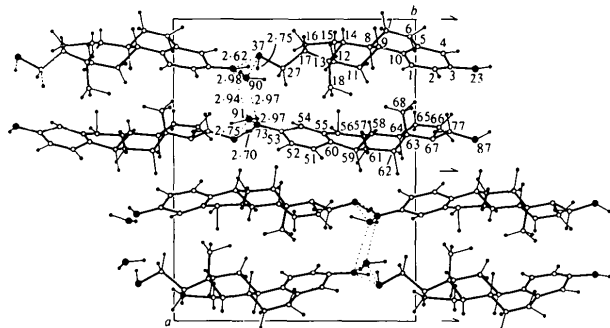
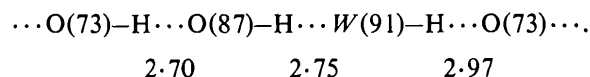


Fig. 3. Projection of the structure along *c*.

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### 4,5-Dihydro-5-hydroxy-4-oxo-5-(2-oxopropyl)-1*H*-pyrrolo[2,3-*f*]quinoline-2,7,9-tricarboxylic Acid Dihydrate

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**Abstract.**  $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_9 \cdot 2\text{H}_2\text{O}$ ,  $M_r = 424.3$ , triclinic,  $P\bar{1}$ ,  $a = 8.593$  (1),  $b = 10.702$  (2),  $c = 10.265$  (2)  $\text{\AA}$ ,  $\alpha = 101.78$  (2),  $\beta = 107.77$  (2),  $\gamma = 91.48$  (2) $^\circ$ ,  $V = 876.1$   $\text{\AA}^3$ ,  $Z = 2$ ,  $D_m = 1.61$  (tetrachloroethane/dibromoethane),  $D_c = 1.61$   $\text{Mg m}^{-3}$ ,  $\mu(\text{Cu } K\alpha) = 1.07$   $\text{mm}^{-1}$ . The final  $R = 0.040$  for 2321 observed reflections. The crystal packing fully utilizes the hydrogen-bonding potential of the molecule.

**Introduction.** The primary alcohol dehydrogenases of methylotrophic bacteria contain a novel cofactor which may have a more general function in the oxidation of organic compounds lacking C—C bonds (Anthony & Zatman, 1967; Sperl, Forrest & Gibson, 1974). The

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Dispersion forces between the different sheets are supplemented by weak hydrogen bonds:  $\text{O}(73)\dots\text{W}(90)$  2.97,  $\text{O}(23)\dots\text{W}(91)$  2.94  $\text{\AA}$ .

Molecules of water have an important role in the crystal packing and we also feel that they play a significant part in hormone–receptor interactions.

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cofactor is released on denaturing the holoenzyme but spontaneously decomposes in water (Sperl, 1973). This process appears to be accelerated in the presence of acetone. Treatment with acetone during the attempted purification led to the isolation of the derivative (I) whose structure is described here. Orange efflorescent needles were obtained by evaporation of an acidic aqueous solution.

