[*e.g.* C(10)–C(11) = 1·477 (5) and C(12)–C(16) = 1·466 (6) Å] due to the formation of the short intramolecular C–H···O interaction.

The two flanking rings in the tricyclic moiety take up planar conformations while the central ring has a 'twist-boat' conformation. The molecules in the crystal structure are held together by van der Waals interactions.

We thank Drs M. S. C. Rao and G. S. Krishna Rao for providing the sample.

References

BRÜCKNER, S., MALPEZZI, L., PROSYANIK, A. V. & BONDARKENKO, S. V. (1985). *Acta Cryst.* C**41**, 215–219.

CHIESI VILLA, A., GAETANI MANFREDOTTI, A., GUASTINI, C., CASIRAGHI, G. & SARTORI, G. (1979). *Cryst. Struct. Commun.* **8**, 639–644.

GANTZEL, P. K., SPARKS, R. A. & TRUEBLOOD, K. N. (1961). *LALS*. A program for the full-matrix refinement of positional and thermal parameters, and scale factors. Univ. of California, USA.

International Tables for X-ray Crystallography (1974). Vol. III. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN*78. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

MOLINS, P., RIUS, J., MIRAVITLLES, C. & BLADE-FONT, A. (1985). *Acta Cryst.* C**41**, 1232–1235.

RAO, M. S. C. & KRISHNA RAO, G. S. (1986). Personal communications.

SURCOUF, E., MORNON, J. P. & MALGRANGE, C. (1978). *Acta Cryst.* B**34**, 2169–2172.

TAYLOR, R. & KENNARD, O. (1982). *J. Am. Chem. Soc.* **104**, 5063–5070.

Acta Cryst. (1989). C**45**, 930–932

11β-Hydroxy-9β-estrone

BY WILLIAM L. DUAX, JANE F. GRIFFIN, PHYLLIS D. STRONG AND KENNETH J. WOOD

Medical Foundation of Buffalo, Inc., 73 High Street, Buffalo, New York 14203, *USA*

(*Received* 2 *August* 1988; *accepted* 3 *January* 1989)

Abstract. $C_{18}H_{22}O_3$, $M_r = 286{\cdot}37$, trigonal, $P3_2$, $a = 10{\cdot}091\ (1)$, $c = 12{\cdot}271\ (1)$ Å, $V = 1082{\cdot}1$ Å^3, $Z = 3$, $D_x = 1{\cdot}318$ Mg m^{-3}, $\lambda(\text{Cu } K\alpha) = 1{\cdot}5418$ Å, $\mu = 0{\cdot}667$ mm^{-1}, $T = 298$ K, $F(000) = 462$, final $R = 0{\cdot}056$ for 1468 observed reflections. The pattern of intermolecular interaction associated with 11β-hydroxy substitution differs from that observed in more potent estrogens.

Introduction. Compounds that bind to the estrogen receptor exhibit a remarkable variability in composition and stereochemistry. On the basis of an examination of a number of these compounds we have proposed that a phenolic ring is critical to the initiation of estrogen receptor binding (Duax, Griffin & Ebright, 1985). 11-Keto-9β-estrone was determined to be a more potent estrogen than its 11β-hydroxy analogue (Segaloff, Gabbard, Flores, Borne, Baker, Duax, Strong & Rohrer, 1980). The X-ray analysis of these compounds was undertaken as part of a program to define further the structural features that control estrogen receptor binding and activity. The X-ray studies were undertaken to verify the stereochemistry of the compounds and to determine how the different substitutions at C(11) alter the overall shape of the steroids and their intermolecular interactions.

Experimental. Colourless crystals from acetone; crystal size: 0·48 × 0·72 × 0·8 mm; symmetry from photographs: $P3_1$ or $P3_2$; $P3_2$ was chosen after the structure was solved on the basis of known enantiomorph; Enraf–Nonius CAD-4 diffractometer; graphite-monochromated Cu $K\alpha$ radiation; cell parameters refined by a least-squares fit of 24 reflections $71 \le 2\theta \le 75°$; 1481 unique reflections ($0 \le h \le 13$, $0 \le k \le 13$, $0 \le l \le 15$, $2\theta \le 75°$), 1468 observed reflections [$I > 2\sigma(I)$], corrected for Lp, no absorption correction applied: $\omega/2\theta$ scan mode, scan angle $(0{\cdot}65 + 0{\cdot}14\tan\theta)°$, scan aperture $(2{\cdot}00 + 0{\cdot}15\tan\theta)$ mm, maximum scan time 90 s, 3 orientation control reflections ($1,\bar{1},\bar{1}0$, $\bar{1}\bar{7}3$, $7\bar{1}1$) monitored every 100 reflections, these reflections were used to check intensity decay; structure solved by direct methods (*MULTAN*78; Main, Hull, Lessinger, Germain, Declercq & Woolfson, 1978); full-matrix least-squares refinement on F for non-hydrogen atoms with anisotropic thermal parameters to minimize $\sum w\Delta^2$, where $w = 1/\sigma_F^2$; all H atoms located in difference synthesis; further refinement with isotropic thermal

0108-2701/89/060930-03$03.00

Table 1. *Fractional positional parameters* ($\times 10^4$) *and equivalent isotropic atomic displacement parameters* ($B \times 10$ Å^2) *for the non-hydrogen atoms with e.s.d.'s in parentheses*

	x	y	z	B_{eq}*
C(1)	7896 (3)	4278 (3)	6885 (3)	25 (1)
C(2)	7674 (4)	5448 (4)	7253 (3)	28 (1)
C(3)	8470 (4)	6891 (4)	6768 (3)	28 (1)
C(4)	9504 (3)	7132 (4)	5937 (3)	29 (1)
C(5)	9727 (3)	5955 (3)	5564 (3)	24 (1)
C(6)	10863 (4)	6307 (4)	4653 (3)	29 (1)
C(7)	10690 (4)	4874 (4)	4088 (3)	30 (1)
C(8)	10555 (3)	3700 (3)	4933	24 (1)
C(9)	9061 (3)	3136 (3)	5597 (3)	23 (1)
C(10)	8914 (3)	4477 (3)	6031 (3)	23 (1)
C(11)	8942 (3)	2007 (3)	6494 (3)	23 (1)
C(12)	10352 (3)	2578 (3)	7226 (3)	22 (1)
C(13)	11822 (3)	3188 (3)	6567 (3)	21 (1)
C(14)	11887 (3)	4366 (3)	5732 (3)	21 (1)
C(15)	13549 (3)	5141 (4)	5303 (3)	27 (1)
C(16)	14457 (4)	5336 (4)	6360 (4)	35 (1)
C(17)	13316 (3)	4165 (3)	7162 (3)	25 (1)
C(18)	12015 (4)	1876 (4)	6070 (3)	29 (1)
O(3)	8169 (3)	7980 (3)	7141 (3)	35 (1)
O(11β)	8643 (3)	577 (2)	5992 (3)	28 (1)
O(17)	13603 (3)	4067 (3)	8110 (3)	35 (1)

* $B_{eq} = \frac{1}{3}$ trace B_{ij}.

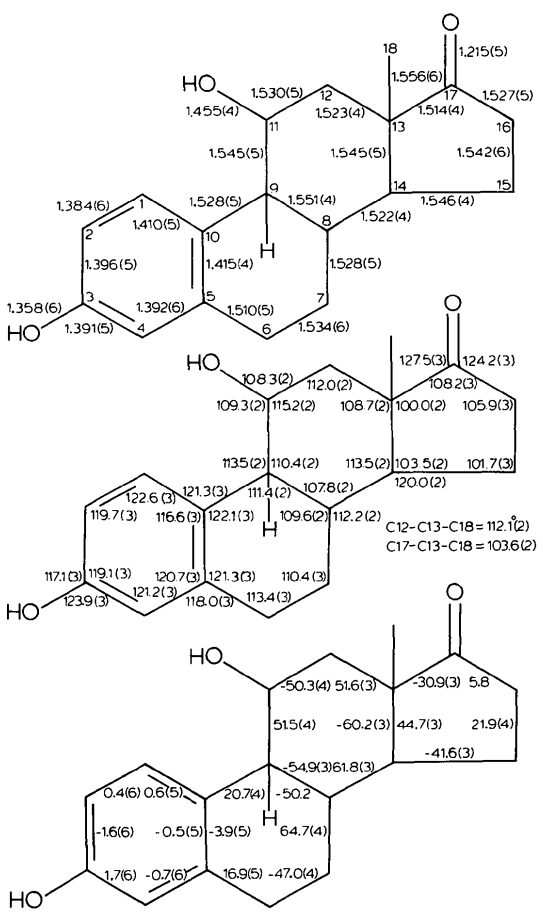

Fig. 1. Selected bond lengths (Å), angles (°) and torsion angles (°) in 11β-hydroxy-9β-estrone.

parameters for H and anisotropic thermal parameters for non-hydrogen atoms; $R = 0.056$, $wR = 0.079$, $S = 2.7$, scattering factors from *International Tables for X-ray Crystallography* (1974). Maximum fluctuation in final difference map -0.39 to 0.28 e Å^{-3}.

Discussion. The atomic positional and isotropic atomic displacement parameters for non-hydrogen atoms in 11β-hydroxy-9β-estrone are given in Table 1.* The bond distances, valence angles, and torsion angles, shown in Fig. 1, were compared with the corresponding geometric parameters on the 11-keto analogue previously studied (Segaloff *et al.*, 1980). The differences (Δ) between corresponding interatomic distances for the non-hydrogen atoms in the two structures are within two standard deviations of one another ($\Delta_{max} = 0.013$ Å, $\Delta_{ave} = 0.007$ Å). The largest differences between corresponding bond angles in the two structures [4·1, 3·2, and 4·1° for C(10)–C(9)–C(11), C(9)–C(11)–C(12), and C(11)–C(12)–C(13), respectively] can be directly attributed to the altered geometry at C(11) associated with the different substituent.

A comparison of the torsion angles involving non-hydrogen atoms in the two structures reveals differences of between 5 and 9° in twenty-five of them. Most of these differences involve atoms in the *C* ring. Five of the largest differences (7° or more) are associated with the conformation of the C(18) methyl group and are a consequence of diaxial interactions between this methyl and the 11β-hydroxy substituent present in one structure but not the other. Despite these significant differences in geometric details caused by the variation in substituents on C(11), the overall shapes of 11-keto-9β-estrone and 11β-hydroxy-9β-estrone are nearly identical. The similarity in overall shape is illustrated in Fig. 2.

Structures containing hydroxyl groups will usually crystallize in such a way as to utilize all hydroxyls in

* Lists of anisotropic thermal parameters, hydrogen-atom coordinates and structure factors, and internal geometry and crystal structure diagrams, have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51707 (13 pp.). Copies may be obtained through The Executive Secretary International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

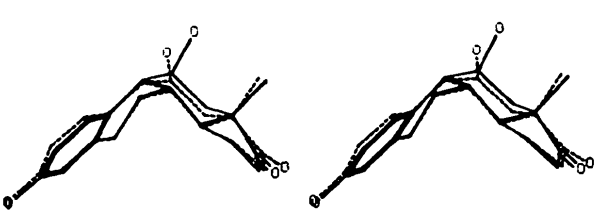

Fig. 2. Superimposed fit of 11-keto-9β-estrone (solid) and 11β-hydroxy-9β-estrone (dashed) from C1 to C18 including O3 and O17.

the formation of hydrogen bonds. As would be expected, both hydroxyl groups in 11β-hydroxy-9β-estrone form hydrogen bonds [O(3)→O(11β) = 2·80 Å, O(3)–H···O(11β) = 131·5°; O(11β)→O(17) = 2·82 Å, O(11β)–H···O(17) = 176·1°] in spite of the fact that the hydrogen-bond angle in one is far from linear. The lone hydrogen bond in 11-keto-9β-estrone [O(3)→O(17) = 2·80 Å, O(3)–H···O(17) = 166·1°] is of the head-to-tail type most commonly observed in steroid structures (Duax & Norton, 1975). The 11β-hydroxyl group disrupts the normal head-to-tail pattern and acts as a donor and an acceptor of hydrogen bonds (Fig. 3). This difference in intramolecular interaction between the 11β-hydroxy group and the 11-oxo atom which accepts no hydrogen bonds and has only normal van der Waals contacts with its surroundings is the most significant difference noted between the structures.

Since the overall shapes and relative positions of the O(3) and O(17) substituents are nearly identical in 11β-hydroxy-9β-estrone and 11-keto-9β-estrone, the activity difference between the two is likely to be a direct consequence of molecular interaction of their C(11) substituents. The fact that the 11β-hydroxy substrate forms strong hydrogen bonds and disrupts normal patterns in steroid association in the solid state may indicate that comparable hydrophilic and hydrogen-bonding interactions interfere with the ability of the compound to function as a potent estrogen.

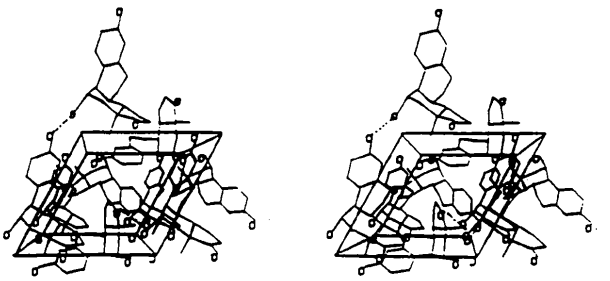

Fig. 3. Stereoview of the crystal structure of 11β-hydroxy-9β-estrone viewed down the *c* axis.

A sample of the title compound was generously provided by the late Dr A. Segaloff. This work was supported by Grant No. AM26546 from the National Institutes of Diabetes and Digestive and Kidney Diseases.

References

DUAX, W. L., GRIFFIN, J. & EBRIGHT, R. (1985). *Molecular Basis of Cancer*. Part B, edited by R. REIN, pp. 263–273. New York: Alan R. Liss.

DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steroid Structure*, Vol. 1, New York: Plenum.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)

MAIN, P., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1978). *MULTAN*78. *A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.

SEGALOFF, A., GABBARD, R. B., FLORES, A., BORNE, R. F., BAKER, J. K., DUAX, W. L., STRONG, P. D. & ROHRER, D. C. (1980). *Steroids*, **35**, 335–349.

Acta Cryst. (1989). C**45**, 932–935

Functionalized Macrocarbocyclic Rings. I. Two Fourteen-Membered Dimethyl Macrocycles with *trans, cis* Diene and *cis* Dienophile

BY ANDRÉ G. MICHEL* AND NADINE MICHEL-DEWEZ

Laboratoire de chimie structurale, Université de Sherbrooke, Sherbrooke (Québec), Canada J1K 2R1

ANDREW L. ROUGHTON

Laboratoire de chimie organique, Université de Sherbrooke, Sherbrooke (Québec), Canada J1K 2R1

AND JAMES P. SPRINGER AND KARST HOOGSTEEN

Merck & Company, Rahway, NJ 07065, *USA*

(*Received* 17 *October* 1988; *accepted* 6 *December* 1988)

Abstract. $C_{24}H_{34}O_8$, $M_r = 450{\cdot}53$, $D_x = 1{\cdot}23$ Mg m^{-3}, λ(Cu $K\bar{\alpha}$) = 1·5418 Å, room temperature. (I) Tetramethyl (3*Z*,5*E*,11*Z*)-3,11-dimethylcyclotetradeca-3,5,11-triene-1,1,8,8-tetracarboxylate, monoclinic, $P2_1/c$, $a = 16{\cdot}025$ (5), $b = 9{\cdot}919$ (4), $c = 16{\cdot}997$ (8) Å, $\beta = 115{\cdot}60$ (4)°, $V = 2436{\cdot}49$ Å^3, $Z = 4$, $\mu =$

* To whom correspondence should be addressed.

0108-2701/89/060932-04$03.00