Pérez, S. & Brisse, F. (1977*a*). *Acta Cryst.* B**33**, 1673–1677.

Pérez, S. & Brisse, F. (1977*b*). *Acta Cryst.* B**33**, 3259–3262.

Sheldrick, G. M. (1976). *SHELX*. A program for crystal structure determination. Univ. Chemical Laboratory, Cambridge, England.

Sundararajan, P. R., Labrie, P. & Marchessault, R. H. (1975). *Can. J. Chem.* **53**, 3557–3562.

Sutton, L. E. (1965). *Interatomic Distances and Configuration in Molecules and Ions*. Spec. Publ. No. 18. London: The Chemical Society.

Ugozzoli, F. (1981). Private communication.

Wilson, A. J. C. (1952). *Nature (London)*, **150**, 151–152.

Yokouchi, M., Sakakibara, Y., Chatani, Y., Tadokoro, H., Tanaka, T. & Yoda, K. (1976). *Macromolecules*, **9**, 266–273.

Acta Cryst. (1982). B**38**, 3139–3142

2α,17α-Bis(2-chloroethynyl)-*A*-nor-5α-œstrane-2*β*,17*β*-diol–Methanol (1/2)

By F. Baert,* M. Foulon and G. Odou

Equipe de Dynamique des Cristaux Moléculaires associée au CNRS (nº 465), *Université des Sciences et Techniques de Lille* I, 59655-*Villeneuve d'Ascq CEDEX, France*

(*Received* 5 *January* 1982; *accepted* 21 *June* 1982)

Abstract. $C_{21}H_{26}Cl_2O_2.2CH_4O$, triclinic, space group $P1$, $a = 8{\cdot}438$ (15), $b = 10{\cdot}339$ (17), $c = 7{\cdot}155$ (15) Å, $\alpha = 98{\cdot}37$ (6), $\beta = 92{\cdot}83$ (4), $\gamma = 97{\cdot}02$ (6)°, $Z = 1$. The structure was determined from 1896 independent intensities and refined to $R = 0{\cdot}049$. Two molecules of CH_3OH (from the solvent of crystallization) are linked by hydrogen bonds to the hydroxyl groups.

Introduction. New derivatives of *A*-nor-5α-œstrane substituted on positions 2 and 17 (or 16) (Canceill, Gasc, Nedelec, Baert, Foulon & Jacques, 1979; Canceill & Jacques, 1980) with hydroxy, ethynyl or chloroethynyl groups have been described and their affinities for various hormonal receptors have been measured (Canceill, Azadian-Boulanger, Philibert, Raynaud & Jacques, 1977). The ability of these steroids to bind to the œstrogenic or androgenic receptors seems governed to a large extent by the 2-hydroxy group being in the α or *β* position. However, the establishment of the stereochemistry of these compounds by chemical methods is not simple.

In the corresponding *A*-norandrostane series the configuration of the 2-hydroxy group has been previously inferred from ^1H NMR and confirmed by ORD data (Jacques, Minssen, Varech & Basselier, 1965). In the *A*-norœstrane series, owing to the lack of the 19-methyl group, this methodology was inapplicable. This difficulty justifies the X-ray crystallographic study reported in the present paper. Moreover, our results confirm the validity of the solution of the same problem deduced from the circular dichroism properties of the 2,16 and 2,17 benzoate derivatives of analogous steroid compounds, in the light of the exciton chirality method (Canceill, Collet & Jacques, 1981).

Experimental. The isomer studied {melting point 410 K and $[\alpha]^{25\,^{\circ}C}_{578} = -8°$} was recrystallized from $CHCl_3$. Well shaped crystals are obtained by slow evaporation in CH_3OH. They decompose rapidly in air.

A single crystal with dimensions $0{\cdot}3 \times 0{\cdot}5 \times 0{\cdot}4$ mm, surrounded by its mother liquor, was sealed in a glass capillary and mounted on a four-circle Philips diffractometer. Intensities for 3728 reflections were measured by the ω–2θ scan and the width of the scan was fixed at 1·6°. The data were corrected for Lorentz–polarization, but not for absorption or extinction. 1896 reflections with $I \geq 3\sigma(I)$ were used in the determination of the structure.

The structure was solved with *MULTAN* (Germain, Main & Woolfson, 1971) based on 200 reflections with $E \geq 1{\cdot}1$. The E map corresponding to the solution with the highest combined figure of merit provided the positions of all the atoms of the molecule except those of the chloroethynyl groups. A Fourier map including all the structure factors showed the missing atoms; however, the Cl atoms appeared as rather weak peaks.

Difference Fourier syntheses clearly indicated two molecules of solvent (CH_3OH) in the vicinity of the OH groups. Subsequent difference syntheses revealed all the H atoms attached to rings *A*, *B*, *C*, *D* and some H atoms of the methyl group in the 17 position. Despite the hydrogen bond which links the methanol molecule to the hydroxyl group, it was impossible to find all the H atoms of the solvent molecules. The final R at the end of the refinement was 0·049 with unit weights.

---

* To whom correspondence should be addressed.

0567-7408/82/123139-04$01.00

The final atomic parameters are listed in Table 1.* The scattering factors for the heavy atoms were those of *International Tables for X-ray Crystallography* (1974); for the H atoms we used those of Stewart, Davidson & Simpson (1965).

The absolute values of peaks and troughs in the final difference map did not exceed 0·2 e Å^{-3}.

Table 1. *Fractional positional parameters* (×10^4) *and* U_{eq} *values* (×10^4)

$U_{\rm eq} = \frac{1}{3}\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j$. Values in parentheses are the anisotropicity defined by $[\sum(U_{\rm eq}-{\rm U}_{ii})^{2/3}]^{1/2}$.

	x	y	z	$U_{\rm eq}$ (Å^2)
Cl(1)	6387 (3)	3282 (3)	4223 (4)	122 (13)
Cl(2)	15165 (3)	11408 (2)	8682 (4)	114 (17)
C(10)	9009 (7)	10343 (5)	3253 (8)	48 (5)
C(8)	7541 (7)	8601 (5)	776 (9)	46 (4)
C(7)	9057 (7)	8571 (6)	−326 (10)	53 (5)
C(9)	7910 (6)	9031 (5)	2908 (9)	43 (5)
C(5)	10513 (7)	10287 (5)	2211 (8)	48 (3)
C(14)	6492 (7)	7253 (5)	488 (9)	48 (2)
C(20)	5524 (8)	4212 (6)	2934 (10)	67 (8)
C(11)	6384 (7)	9049 (6)	3983 (9)	59 (5)
C(4)	11508 (8)	11598 (6)	2952 (10)	65 (7)
C(1)	9692 (7)	10849 (6)	5264 (9)	63 (6)
C(12)	5317 (6)	7730 (6)	3615 (8)	55 (9)
C(17)	4190 (7)	5803 (6)	914 (10)	58 (9)
C(13)	4938 (6)	7281 (6)	1499 (9)	51 (11)
C(19)	4955 (7)	4922 (5)	2022 (9)	57 (6)
C(6)	10173 (7)	9914 (6)	107 (8)	58 (6)
O(2)	10760 (5)	13203 (4)	5468 (7)	73 (14)
C(15)	5979 (7)	6538 (6)	−1514 (9)	61 (9)
O(17)	2489 (4)	5580 (4)	1045 (6)	68 (17)
C(2)	11157 (7)	11891 (6)	5059 (9)	57 (3)
C(16)	4542 (8)	5523 (6)	−1223 (10)	64 (6)
C(22)	13612 (8)	11582 (7)	7299 (11)	71 (6)
C(21)	12517 (8)	11735 (6)	6301 (10)	62 (7)
C(18)	3801 (7)	8140 (7)	665 (10)	76 (18)
O(3)	1633 (7)	5655 (5)	4602 (8)	101 (24)
O(4)	267 (6)	3739 (6)	9126 (8)	102 (29)
C(24)	−1136 (9)	14051 (11)	9901 (15)	114 (53)
C(23)	547 (11)	6450 (8)	5503 (15)	127 (18)

Thermal-vibration analysis. Fig. 1 gives a perspective view of the molecule. The thermal-ellipsoid axes of the atoms of the two ethynyl groups have peculiar orientations with respect to the bonds. An analysis of the thermal vibrations in rigid-body terms was undertaken (Schomaker & Trueblood, 1968) to gain a better understanding of the thermal agitation of the molecule in the crystal.

Three rigid-body models were used, the first (I) consisting of all the heavy atoms belonging to the molecule; in the second model (II) the two Cl atoms were omitted, and in the third (III) the two chloroethynyl groups were omitted.

We observed that the steroid nucleus (model III) does in fact behave very nearly as a rigid body. The root-mean-square differences between the observed U_{ij} terms and those calculated from the derived **T**, **L** and **S** are only 0·0051 Å^2.

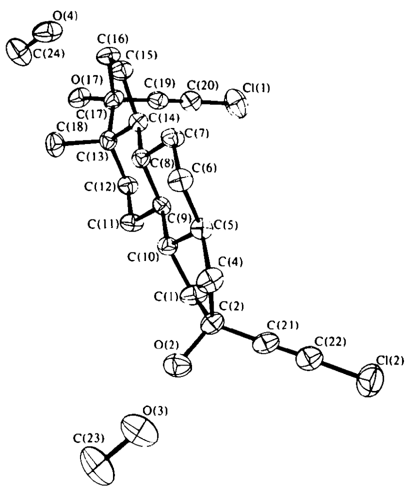

Fig. 1. Perspective view of the molecule.

Table 2. *Rigid-body-vibration parameters for the heaviest atoms of the molecules*

Model I: the whole molecule. Model II: Cl atoms not included. Model III: without chloroethynyl groups.

	Model I			Model II			Model III		
T (Å^2) (×10^4)	425 (27)	27 (23)	83 (35)	423 (18)	−1 (16)	79 (17)	392 (17)	38 (17)	41 (16)
		490 (24)	21 (23)		492 (17)	−17 (16)		469 (19)	4 (16)
			439 (30)			448 (19)			446 (19)
L (rad^2) (×10^4)	25 (3)	18 (3)	7 (2)	22 (3)	16 (3)	8 (2)	36 (5)	32 (4)	12 (3)
		33 (3)	9 (2)		28 (3)	6 (2)		46 (5)	11 (3)
			17 (2)			17 (2)			24 (3)
S (Å rad) (×10^5)	−41 (84)	−5 (60)	−64 (58)	−4 (61)	47 (43)	126 (43)	11 (71)	18 (45)	178 (52)
	11 (61)	−37 (88)	−30 (60)	44 (46)	−86 (64)	171 (45)	−74 (51)	−127 (67)	225 (53)
	−75 (44)	−84 (45)	78 (97)	−134 (32)	−129 (32)	90 (630)	−129 (36)	−152 (33)	116 (55)
r.m.s. (U^o-U^c) (Å^2)		0·0091			0·0058			0·0051	
e.l.d. $U_{ii}^{\rm obs}$ (Å^2)		0·0098			0·0063			0·0056	

---

* Lists of structure factors, H-atom coordinates and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38025 (19 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. *Bond lengths* (Å) *before and after libration correction for the heavy atoms, and bond angles* (°), *with e.s.d.'s in parentheses*

	Uncorrected	Corrected		Uncorrected	Corrected
C(1)–C(2)	1·565 (8)	1·567	C(14)–C(13)	1·530 (8)	1·534
C(2)–C(4)	1·545 (10)	1·549	C(13)–C(12)	1·524 (9)	1·528
C(4)–C(5)	1·514 (8)	1·516	C(12)–C(11)	1·521 (8)	1·523
C(5)–C(10)	1·507 (8)	1·511	C(11)–C(9)	1·533 (9)	1·537
C(10)–C(1)	1·517 (8)	1·520	C(14)–C(15)	1·529 (8)	1·533
C(2)–O(2)	1·429 (7)	1·433	C(15)–C(16)	1·547 (9)	1·550
C(2)–C(21)	1·455 (9)	1·459	C(16)–C(17)	1·565 (10)	1·569
C(21)–C(22)	1·180 (10)	1·184	C(17)–C(13)	1·569 (8)	1·571
Cl(2)–C(22)	1·646 (8)	1·651	C(17)–O(17)	1·436 (7)	1·439
C(5)–C(6)	1·503 (8)	1·507	C(17)–C(19)	1·476 (9)	1·481
C(6)–C(7)	1·562 (8)	1·564	C(19)–C(20)	1·178 (10)	1·182
C(7)–C(8)	1·536 (9)	1·541	C(20)–Cl(1)	1·633 (8)	1·639
C(8)–C(9)	1·531 (9)	1·535	C(13)–C(18)	1·540 (9)	1·545
C(9)–C(10)	1·527 (7)	1·529	O(3)–C(13)	1·420 (11)	
C(8)–C(14)	1·538 (7)	1·540	O(4)–C(24)	1·386 (11)	

Cl(2)–C(22)–C(21)	178·5 (7)	C(22)–C(21)–C(2)	178·7 (6)
C(1)–C(2)–C(4)	104·2 (5)	C(1)–C(2)–O(2)	111·1 (5)
C(1)–C(2)–C(21)	110·6 (5)	C(21)–C(2)–O(2)	110·0 (5)
C(21)–C(2)–C(4)	111·6 (5)	C(2)–C(4)–C(5)	105·0 (5)
C(4)–C(5)–C(6)	118·2 (5)	C(5)–C(10)–C(1)	101·3 (5)
C(5)–C(10)–C(9)	112·4 (5)	C(1)–C(10)–C(9)	117·5 (5)
C(10)–C(9)–C(8)	109·4 (5)	C(10)–C(9)–C(11)	113·6 (5)
C(11)–C(9)–C(8)	112·1 (5)	C(9)–C(8)–C(7)	112·8 (5)
C(8)–C(7)–C(6)	111·6 (5)	C(7)–C(6)–C(5)	109·5 (5)
C(10)–C(5)–C(6)	112·5 (5)	C(9)–C(11)–C(12)	112·4 (5)
C(11)–C(12)–C(13)	110·9 (5)	C(12)–C(13)–C(14)	109·9 (4)
C(12)–C(13)–C(18)	112·5 (5)	C(12)–C(13)–C(17)	115·6 (5)
C(13)–C(14)–C(8)	112·9 (5)	C(13)–C(14)–C(15)	104·9 (5)
C(8)–C(14)–C(15)	120·0 (5)	C(7)–C(8)–C(14)	112·2 (5)
C(17)–C(13)–C(14)	99·5 (4)	C(14)–C(15)–C(16)	103·7 (5)
C(15)–C(16)–C(17)	106·8 (5)	C(16)–C(17)–C(13)	102·4 (5)
C(13)–C(17)–O(17)	113·9 (5)	C(13)–C(17)–C(19)	111·8 (5)
C(16)–C(17)–C(19)	111·1 (5)	C(19)–C(17)–O(17)	109·1 (5)
C(17)–C(19)–C(20)	178·0 (7)	C(19)–C(20)–Cl(1)	177·2 (6)

We noticed that the methyl substituent has a small amount of additional independent motion. The elements of the tensors **T**, **L** and **S** are given in Table 2. There is an increase in rotational motion between models II and III; however, the root-mean-square differences ($U^o - U^c$) in these two models are very close. On the other hand, including the Cl atoms produced an anchorage effect with large discrepancies between the U^o and U^c. As the **T** and **L** values are almost identical in models I and II it seems reasonable to postulate that the Cl atoms undergo important internal and torsional motions of low frequencies which of course could reduce the contributions of these atoms to the structure factors. These remarks are in agreement with the very large values of the Debye–Waller factor, and could explain the reasons for not finding the Cl atoms in the direct-method analysis.

The amplitudes of libration of model I were used to correct the effects of rigid-body motion on the bond lengths (Busing & Levy, 1964). The values are reported in Table 3.

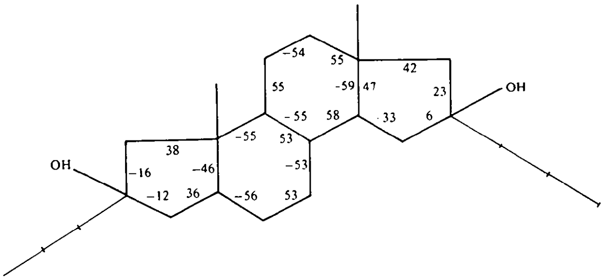

Fig. 2. Ring torsion angles (°). $\bar{\sigma} = 0{\cdot}5$°.

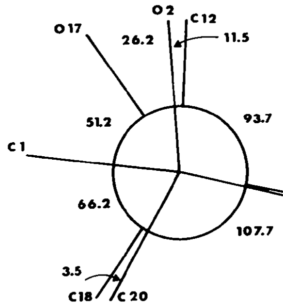

Fig. 3. Newman projection along the direction C(2)–C(17). Angles are in deg. $\bar{\sigma} = 0{\cdot}5$°.

Discussion. The bond lengths in Table 3 are close to the values of the 2α,16α-diethynyl derivative reported by Mornon, Lepicard, Delettré, Bally & Brassy (1982). However, the geometry of the 2α,16α molecule is more bent than that of the *A*-nor 2,17-bis(dichloroethynyl) molecule (Fig. 2), and this curvature could be due to the simultaneous presence of methyl groups in the 18 and 19 positions. The torsion angles (Fig. 2) underline this feature. The perspective view shows clearly that the two OH groups in positions 2 and 17 occupy the *β* position. The two chloroethynyl groups are *trans* with respect to the ring. A Newman projection (Fig. 3) along the line C(2)–C(17) shows that the two hydroxyl groups are in staggered positions with an angle of 26°.

No intermolecular distances are less than the sum of the van der Waals radii, except for the hydrogen bonds between the hydroxyl groups and the molecules of solvent.

The authors are grateful to Ms J. Canceill and Professor J. Jacques for proposing this interesting problem and providing the crystals.

This work was supported by the Centre National de la Recherche Scientifique.

References

Busing, W. R. & Levy, H. A. (1964). *Acta Cryst.* **17**, 1040–1044.

Canceill, J., Azadian-Boulanger, G., Philibert, D., Raynaud, J. P. & Jacques, J. (1977). *C.R. Acad. Sci. Sér. C*, **285**, 37–40.

Canceill, J., Collet, A. & Jacques, J. (1981). *J. Chem. Soc. Perkin Trans.* 2. In the press.

Canceill, J., Gasc, J. C., Nedelec, L., Baert, F., Foulon, M. & Jacques, J. (1979). *Bull. Soc. Chim. Fr.* pp. 157–164.

Canceill, J. & Jacques, J. (1980). *Bull. Soc. Chim. Fr.* pp. 468–472.

Germain, G., Main, P. & Woolfson, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

Jacques, J., Minssen, M., Varech, D. & Basselier, J. J. (1965). *Bull. Soc. Chim. Fr.* pp. 77–87.

Mornon, J. P., Lepicard, G., Delettré, J., Bally, R. & Brassy, C. (1982). *Acta Cryst.* B**38**, 2973–2975.

Schomaker, V. & Trueblood, K. N. (1968). *Acta Cryst.* B**24**, 63–76.

Stewart, R. F., Davidson, E. R. & Simpson, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

Acta Cryst. (1982). B**38**, 3142–3144

Structure of 4-Fluoro-1,3,5(10)-estratriene-3,17β-diol–Hemimethanol

By Kuantee Go, Gopinath Kartha and Moshe Neeman

Roswell Park Memorial Institute, 666 Elm St, Buffalo, NY 14263, USA

(*Received 8 February 1982; accepted 25 June 1982*)

Abstract. $C_{18}H_{23}FO_2.\frac{1}{2}CH_3OH$, triclinic, $P1$, $a = 7{\cdot}367\,(1)$, $b = 9{\cdot}363\,(6)$, $c = 12{\cdot}531\,(1)$ Å, $\alpha = 89{\cdot}31\,(3)$, $\beta = 93{\cdot}38\,(1)$, $\gamma = 109{\cdot}62\,(3)^\circ$, $V = 812{\cdot}8$ Å^3, $Z = 2$. The structure was solved by direct methods and refined by block-diagonal least squares to an R factor of 6·2% for 3043 observed reflections. The general features of the steroid are similar to those of other estratriene analogs. Molecules in the crystal are linked together in a head-to-tail fashion between the O at C(3) and at C(17), and sideways between the hydroxyls of the solvent and the steroid.

Introduction. Tumor inhibitory effects on estrogen administration have been observed in breast and prostatic cancers and attempts have been made to obtain modified steroidal estrogens that will be useful in cancer chemotherapy. In this connection it is seen that in contrast to the biologically inactive bromo analog, 4-fluoroestratrienediol (4FE2) is a very highly active estrogen. The present crystallographic study of the structure and conformation of 4FE2 was undertaken to establish the stereochemical reason, if any, for the striking difference in biological activity of the two analogs.

A crystal of about 1·3 × 0·8 × 0·3 mm crystallized from benzene was used to collect the diffraction data. The crystals are triclinic with space group $P1$. Lattice parameters were refined by a least-squares fit to a set of 24 measured reflections in a θ range 10–34° (Cu $K\alpha$). Three-dimensional data were collected on an Enraf–Nonius CAD-4 automated diffractometer using Ni-filtered Cu $K\alpha$ radiation by ω–2θ scans within the Cu sphere of 2θ to 150°. The measured intensities were converted to structure amplitudes in the usual manner, and corrected for Lorentz, polarization, and absorption effects. There were 3436 unique reflections measured, of which 3043 had intensities greater than $2\sigma(I)$ and were used in the determination and refinement of the structure.

The space group $P1$ with two molecules of the steroid in the asymmetric unit presented some difficulties in its structure solution. Many initial attempts using the direct-methods program *MULTAN* (Germain, Main & Woolfson, 1971) varying a number of parameters failed to give any phase sets that looked significantly better than any other. All of the phase sets obtained had figures of merit of 1·25 or higher and yielded maps showing repeating hexagonal rings with peaks in the middle of the hexagons also. Recycling procedures starting with many of the molecular fragments picked up by the program failed to develop into the correct model. Of the 20 phase sets calculated using 348 reflections with E values greater than 1·55, only one had a figure of merit less than 1·2 and the map for this set also gave a fragment with fused hexagonal rings. From this, 17 atomic positions were chosen corresponding to three fused hexagonal rings with three additional atoms as in a steroid nucleus. A weighted Fourier map with the 17-atom fragment as input showed another fragment of 12 atoms resembling part of a steroid molecule. The second partial molecule was also included in calculating the next weighted Fourier map which developed into a complete molecule showing the five-membered ring and with 19 of the 21 atoms indicated unambiguously. With these 36 atoms included, the next weighted Fourier map calculation clearly revealed all 42 non-H atoms in the two steroid molecules and also showed the presence of a solvent containing two covalently bonded atoms which was recognized as a methanol molecule and was included in the subsequent refinement. Assignment of atom types and ascribing anisotropic thermal parameters for these 44 atoms and a few more cycles of least-squares refinement gave an R of 8%. At this stage, most of the H positions were located from the difference Fourier maps. Inclusion of all H atoms and a few cycles of least-squares refinement gave a final R of 6·16% for 3043 reflections. The function minimized was $\sum w(|F_o|$

0567-7408/82/123142-03$01.00