Acta Cryst. (1976). B32, 2819

The Crystal and Molecular Structures of Two 9α-Fluoro-2α-methyl Steroids

BY CHARLES M. WEEKS AND WILLIAM L. DUAX

Medical Foundation of Buffalo, 73 High Street, Buffalo, New York 14203, *U.S.A.*

(*Received* 3 *February* 1976; *accepted* 23 *April* 1976)

The crystal structures of 9α-fluoro-2α-methylcortisol (I) ($C_{22}H_{31}FO_5$), and 9α-fluoro-11β-hydroxy-2α-methylprogesterone (II) ($C_{22}H_{31}FO_3$), were determined in order to investigate the effects of the 9α-fluoro and 2α-methyl substituents on the *A* ring conformation and orientation. The *A* rings were found to be bent beneath the *BCD* plane, but the angle of inclination was not as large as in 9α-fluorocortisol. These structures, which crystallize in space group $P2_12_12_1$ with four molecules in the unit cell, are isomorphous, but they have different hydrogen bonds. The cell dimensions are $a=10{\cdot}837$, $b=17{\cdot}629$, $c=10{\cdot}252$ Å for (I) and $a=10{\cdot}614$, $b=17{\cdot}800$, $c=10{\cdot}103$ Å for (II).

Introduction

As a result of crystallographic study, the *A* ring of 9α-fluorocortisol (Dupont, Dideberg & Campsteyn, 1972; Weeks, Duax & Wolff, 1973) was found to be bent far beneath the plane of the *B*, *C* and *D* rings, and this causes the overall molecular shape to resemble structures of the 1,4-pregnadiene type. Structure determinations of 9α-fluoro-2α-methylcortisol* and 9α-fluoro-11β-hydroxy-2α-methylprogesterone* were undertaken in order to see if this conformational feature occurs in other 9α-fluoro steroids. 9α-Fluoro-2α-methylcortisol was also of interest because it has been reported (Hogg, Lincoln, Jackson & Schneider, 1955) to be a more potent mineralocorticoid than the natural hormone aldosterone.

Although the crystal structures of these two 9α-fluoro-2α-methyl steroids are isomorphous, they have different hydrogen bonds. Nine other isomorphous, pairs occur among the approximately 200 steroids of the estrane, androstane and pregnane type for which atomic coordinates have been reported. Most of these isomorphous sets show differences in hydrogen-bonding patterns indicating that hydrogen bonds are not of primary importance in determining steroid packing arrangements.

* Throughout this paper, the trivial name 9α-fluoro-2α-methylcortisol will be used for 9α-fluoro-11β,17α,21-trihydroxy-2α-methyl-4-pregnene-3,20-dione, and the trivial name 9α-fluoro-11β-hydroxy-2α-methylprogesterone will be used for 9α-fluoro-11β-hydroxy-2α-methyl-4-pregnene-3,20-dione.

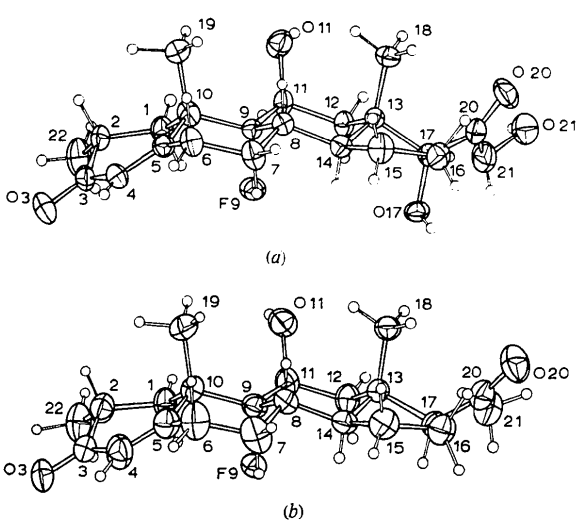

Fig. 1. Conformations of the 9α-fluoro steroids. The atomic numbering and thermal vibration ellipsoids, scaled to 50% probability, of the nonhydrogen atoms are illustrated. (*a*) 9α-Fluoro-2α-methylcortisol (I). (*b*) 9α-Fluoro-11β-hydroxy-2α-methylprogesterone (II).

Experimental

9α-Fluoro-2α-methylcortisol (I) was crystallized from methanol by slow evaporation, and 9α-fluoro-11β-hydroxy-2α-methylprogesterone (II) was crystallized from ethanol. Experimental X-ray measurements were performed on an Enraf–Nonius CAD-4 diffractometer using Cu $K\alpha$ radiation. In both cases, the systematic absences in the diffraction pattern were consistent with the orthorhombic space group $P2_12_12_1$ (D_2^4, No. 19), and the cell constants were determined by a least-squares analysis of the 2θ values for 15 reflections [at 20°C; $\lambda(\text{Cu } K\bar{\alpha})=1{\cdot}54178$ Å]. The densities of the crystals were determined by flotation. The crystal data for the two compounds are summarized in Table 1.

Integrated intensities for 2293 reflections were meas-

Table 1. *Crystal data for* 9α-*fluoro*-2α-*methylcortisol* (I) *and* 9α-*fluoro*-11β-*hydroxy*-2α-*methylprogesterone* (II)

	(I)	(II)
Formula	$C_{22}H_{31}FO_5$	$C_{22}H_{31}FO_3$
M	394·49	362·49
Space group	$P2_12_12_1$	$P2_12_12_1$
Z	4	4
a	10·837 ± 0·001 Å	10·614 ± 0·001 Å
b	17·629 ± 0·001	17·800 ± 0·001
c	10·252 ± 0·001	10·103 ± 0·001
V	1958·6 Å^3	1908·8 Å^3
D_m	1·33 g cm^{-3}	1·20 g cm^{-3}
D_c	1·33	1·26

ured for crystal (I) and 2250 reflections for crystal (II). Lorentz and polarization corrections $[(1+\cos^2 2\theta)/2\sin 2\theta]$ were applied to both sets of intensity data, and normalized structure factor amplitudes were computed. The structure of compound (II) was then solved by a straightforward application of *MULTAN* (Germain, Main & Woolfson, 1971). Since the cell constants for the two compounds were nearly identical, it seemed likely that the structures were isomorphous. Consequently, the coordinates of structure (II) and the data for structure (I) were used to compute a Fourier map, and the locations of the two non-hydrogen atoms, O(17) and O(21), present in structure (I) but missing from structure (II), were clearly visible.

Table 2. *Atomic coordinates* ($\times 10^5$) *and anisotropic thermal parameters* ($\times 10^4$) *for the non-hydrogen atoms*

The thermal parameters are of the form $\exp[-2\pi^2(U_{11}h^2a^{*2}+2U_{12}hka^*b^*+\ldots)]$. The standard deviations of the last two figures are given in parentheses.

(*a*) 9α-Fluoro-2α-methylcortisol

	x	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	55547 (21)	69080 (11)	50096 (23)	342 (10)	268 (9)	398 (11)	6 (8)	−49 (9)	8 (8)
C(2)	64471 (23)	75318 (13)	54440 (25)	399 (11)	296 (9)	443 (12)	−58 (8)	0 (10)	−16 (9)
C(3)	73476 (22)	72329 (13)	64452 (23)	345 (11)	384 (10)	366 (10)	−83 (9)	27 (9)	−56 (9)
C(4)	77499 (22)	64490 (14)	63020 (23)	325 (10)	418 (11)	383 (11)	−17 (9)	−74 (9)	−29 (9)
C(5)	72622 (19)	59606 (12)	54406 (22)	271 (8)	331 (9)	339 (10)	−9 (8)	−11 (6)	−5 (8)
C(6)	78230 (21)	51867 (14)	52463 (29)	286 (10)	386 (11)	564 (13)	41 (8)	−54 (11)	−64 (11)
C(7)	68584 (22)	45555 (13)	53272 (28)	335 (10)	327 (10)	517 (13)	63 (8)	−110 (10)	−2 (10)
C(8)	57421 (19)	46977 (11)	44575 (21)	265 (9)	258 (8)	311 (9)	38 (7)	−14 (7)	−13 (7)
C(9)	52163 (19)	55012 (10)	46826 (19)	280 (8)	254 (8)	254 (8)	17 (7)	4 (7)	−6 (7)
C(10)	61761 (19)	61614 (12)	45679 (20)	318 (9)	284 (8)	279 (9)	−22 (7)	−23 (8)	−4 (8)
C(11)	40102 (20)	56358 (11)	39290 (24)	311 (9)	248 (8)	420 (10)	5 (8)	−69 (9)	50 (8)
C(12)	30346 (20)	50156 (11)	41774 (23)	284 (9)	237 (8)	413 (10)	14 (7)	−35 (8)	8 (8)
C(13)	35431 (19)	42153 (10)	39615 (20)	288 (8)	238 (8)	275 (8)	7 (7)	−5 (8)	−10 (7)
C(14)	47306 (19)	41204 (10)	47571 (21)	299 (9)	233 (8)	301 (8)	37 (7)	−8 (8)	−3 (7)
C(15)	50042 (22)	32659 (12)	46657 (25)	398 (11)	264 (8)	474 (12)	81 (8)	−2 (10)	−10 (9)
C(16)	37034 (24)	28956 (12)	45941 (25)	457 (12)	235 (9)	442 (12)	30 (8)	48 (11)	−22 (9)
C(17)	27729 (20)	35551 (11)	45811 (20)	369 (10)	232 (8)	293 (9)	−9 (7)	41 (8)	−17 (7)
C(18)	37409 (24)	40473 (13)	24963 (22)	440 (12)	387 (11)	285 (9)	−18 (10)	13 (9)	−16 (9)
C(19)	67111 (25)	62570 (16)	31863 (24)	478 (14)	475 (12)	325 (10)	−128 (11)	60 (10)	2 (10)
C(20)	15760 (23)	34052 (12)	38498 (25)	419 (11)	285 (9)	391 (10)	−89 (8)	14 (9)	6 (9)
C(21)	4317 (24)	37845 (16)	43572 (28)	375 (12)	495 (12)	482 (12)	−90 (10)	24 (10)	−31 (11)
C(22)	57454 (29)	82265 (14)	59352 (38)	542 (15)	327 (11)	803 (21)	−10 (11)	−58 (16)	−93 (13)
O(3)	77886 (21)	76323 (11)	72953 (21)	564 (11)	493 (10)	505 (10)	−61 (9)	−83 (9)	−193 (9)
O(11)	43528 (17)	56841 (11)	25915 (18)	417 (9)	511 (9)	378 (8)	−90 (8)	−135 (7)	182 (8)
O(17)	24629 (16)	37708 (9)	58952 (15)	437 (8)	315 (6)	271 (7)	11 (6)	67 (6)	−3 (6)
O(20)	15342 (21)	30207 (12)	28727 (22)	551 (11)	543 (11)	506 (10)	−90 (9)	−23 (9)	−191 (9)
O(21)	−6004 (18)	36902 (15)	35518 (23)	361 (9)	808 (14)	596 (12)	−97 (10)	−49 (9)	39 (12)
F(9)	48453 (12)	55164 (6)	60233 (12)	392 (6)	296 (5)	271 (5)	−11 (5)	58 (5)	−9 (4)

(*b*) 9α-Fluoro-11β-hydroxy-2α-methylprogesterone

	x	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	54177 (21)	69161 (10)	51486 (24)	424 (10)	324 (8)	556 (12)	−15 (8)	−29 (9)	−9 (8)
C(2)	63468 (21)	75477 (12)	54837 (22)	467 (10)	369 (8)	505 (10)	−90 (8)	−4 (9)	35 (9)
C(3)	73434 (23)	72711 (13)	64309 (23)	527 (12)	452 (10)	443 (10)	−143 (9)	−13 (10)	33 (9)
C(4)	77194 (24)	64854 (13)	63156 (26)	482 (12)	496 (11)	617 (13)	−73 (10)	−134 (11)	40 (11)
C(5)	71928 (22)	59950 (12)	54860 (24)	413 (10)	438 (10)	525 (11)	−16 (9)	−20 (10)	1 (9)
C(6)	77724 (23)	52289 (14)	57650 (34)	423 (11)	522 (12)	904 (20)	91 (10)	−61 (13)	−45 (13)
C(7)	68143 (25)	45998 (13)	53645 (31)	529 (13)	435 (11)	758 (17)	103 (10)	−205 (13)	−2 (11)
C(8)	56327 (20)	47422 (11)	45367 (21)	430 (10)	348 (8)	410 (10)	83 (6)	−44 (8)	−12 (7)
C(9)	50775 (18)	55222 (9)	48384 (18)	407 (9)	307 (7)	292 (7)	25 (7)	−4 (7)	−5 (6)
C(10)	60325 (19)	61837 (10)	46642 (20)	386 (9)	345 (8)	375 (8)	−11 (7)	1 (8)	9 (8)
C(11)	37579 (19)	56608 (10)	42231 (20)	391 (9)	269 (7)	427 (9)	28 (7)	−26 (9)	−12 (7)
C(12)	28489 (19)	49996 (10)	44256 (22)	428 (10)	279 (7)	499 (11)	11 (8)	6 (9)	−39 (6)
C(13)	34090 (20)	42382 (10)	40523 (19)	472 (10)	265 (7)	323 (8)	−2 (7)	8 (8)	−2 (7)
C(14)	46421 (22)	41463 (10)	48339 (19)	527 (11)	293 (8)	350 (8)	76 (8)	−20 (9)	15 (7)
C(15)	49728 (25)	33073 (11)	46792 (25)	694 (15)	290 (8)	603 (13)	114 (10)	−69 (12)	57 (9)
C(16)	36725 (28)	29193 (12)	46507 (25)	759 (16)	307 (9)	584 (13)	21 (10)	−18 (13)	56 (9)
C(17)	26635 (23)	35431 (10)	46063 (21)	624 (13)	296 (8)	394 (9)	−47 (9)	58 (10)	18 (8)
C(18)	35949 (24)	41498 (11)	25559 (20)	623 (13)	369 (9)	325 (8)	−21 (9)	−25 (9)	20 (7)
C(19)	64893 (25)	62818 (15)	32126 (23)	611 (14)	567 (13)	440 (11)	−106 (12)	102 (11)	13 (11)
C(20)	14980 (26)	33554 (12)	38423 (25)	669 (14)	366 (10)	537 (12)	−144 (10)	28 (11)	58 (9)
C(21)	3179 (29)	37790 (16)	41901 (33)	599 (15)	657 (15)	780 (17)	−129 (14)	54 (15)	31 (15)
C(22)	56524 (25)	82400 (14)	59851 (34)	598 (14)	389 (10)	894 (20)	−72 (11)	6 (14)	−82 (12)
O(3)	78789 (21)	76881 (9)	72214 (19)	815 (12)	495 (9)	601 (10)	−247 (9)	−160 (10)	21 (8)
O(11)	38639 (16)	58361 (8)	28573 (15)	608 (9)	334 (6)	440 (7)	24 (7)	−117 (7)	61 (6)
O(20)	14817 (23)	28910 (11)	29722 (22)	942 (14)	502 (9)	724 (12)	−167 (10)	−107 (12)	−156 (9)
F(9)	48170 (13)	55112 (6)	62275 (11)	555 (7)	362 (5)	315 (5)	−55 (5)	26 (5)	−23 (4)

The atomic parameters for both compounds were refined by block-diagonal least-squares calculations. After several cycles of anisotropic refinement, Fourier difference maps were computed, and the majority of the hydrogen atoms were located. The remaining hydrogens bonded to carbon atoms were placed at their geometrically expected positions. The parameters for all the atoms including the hydrogens were then refined for six final cycles in the case of compound (I) and for two cycles for compound (II). In both cases, data for which $|F_c|/|F_o|$ was less than 0·5 [51 reflections for compound (I) and 43 reflections for compound (II) during the final cycle] were excluded from the refinement, and the quantities $(1/\sigma_F^2)$ were used as weights where σ_F is as defined by Stout & Jensen (1968, equation H.14) and the instability correction was 0·06 rather than 0·01. This value increases σ_F for reflections with a small $|F|$ and prevents them from controlling the refinement. The R index was defined as $\sum(||F_o|-|F_c||)/\sum|F_o|$. Its final value for all data was 4·8% for compound (I) and 5·0% for compound (II). The final refined positional and anisotropic thermal parameters for the non-hydrogen atoms are given in Table 2, and the positional and isotropic thermal parameters for the hydrogens are listed in Table 3.*

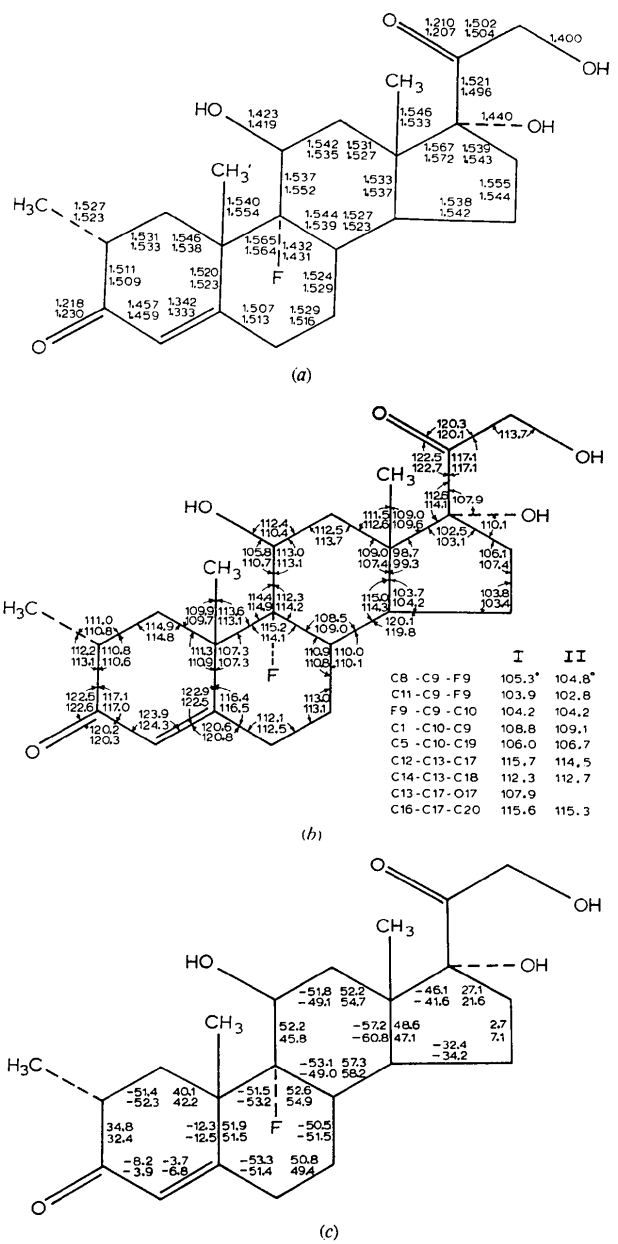

Fig. 2. Intramolecular geometry. The values for structure (I) are given above those for structure (II). (*a*) Interatomic distances (Å). (*b*) Bond angles (°). (*c*) Endocyclic torsion angles (°).

* A list of structure factors has been deposited with the British Library Lending Division as Supplementary Publication No. SUP 31836 (23 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 3. *Final atomic coordinates* ($\times 10^3$) *for the hydrogen atoms*

The average refined value for B_{iso} was 2·8 Å² for 9α-fluoro-2α-methylcortisol (I) and 3·6 Å² for 9α-fluoro-11β-hydroxy-2α-methylprogesterone (II).

	9α-Fluoro-2α-methylcortisol			9α-Fluoro-11β-hydroxy-2α-methylprogesterone		
	x	*y*	*z*	*x*	*y*	*z*
H(1*A*)	493*	680	575	494*	684	604
H(1*B*)	512	707	430	485	712	460
H(2*B*)	696	777	468	688	769	466
H(4*A*)	842	628	680	851	638	693
H(6*A*)	851	507	590	857	516	590
H(6*B*)	818	521	429	808	526	434
H(7*A*)	658	453	618	665	455	627
H(7*B*)	718	402	513	721	419	511
H(8*B*)	603	467	356	587	472	365
H(11*A*)	375	609	429	337	610	467
H(12*A*)	275	506	497	253	496	532
H(12*B*)	237	509	347	203	515	389
H(14*A*)	454	419	564	447	422	569
H(15*A*)	543	309	542	548	317	536
H(15*B*)	552	325	401	547	322	384
H(16*A*)	358	259	522	355	259	550
H(16*B*)	361	259	370	357	263	372
H(17*A*)	–	–	–	244	373	557
H(18*A*)	391	356	229	387	364	232
H(18*B*)	432	440	204	420	450	216
H(18*C*)	315	415	195	287	425	213
H(19*A*)	697	580	291	679	588	290
H(19*B*)	753	665	332	728	668	324
H(19*C*)	611	647	267	586	658	265
H(21*A*)	66	427	450	−36*	350	375
H(21*B*)	30	364	510	25	363	506
H(21*C*)	–	–	–	26*	428	394
H(22*A*)	525	809	660	518	814	673
H(22*B*)	530	833	518	521	843	529
H(22*C*)	629	859	616	633	864	631
H(110)	384	572	228	362	620	274
H(170)	260	340	623	–	–	–

* This hydrogen was placed at its geometrically expected position. In addition, atom H(210) in structure (I) could not be located.

Discussion

The crystallographically observed conformations of 9α-fluoro-2α-methylcortisol (I) and 9α-fluoro-11β-hydroxy-2α-methylprogesterone (II) are shown in Fig. 1, which also illustrates the atomic numbering and the non-hydrogen thermal vibration ellipsoids scaled to 50% probability. Bond distances and angles involving the non-hydrogen atoms are given in Fig. 2. The standard deviations of these measurements are 0·002–0·004 Å and 0·1–0·2° respectively. There are no unusual values. The endocyclic torsion angles are also given in Fig. 2, and a torsion angle α–β–γ–δ is considered positive if, when viewed down the β–γ bond, the α–β bond will eclipse the γ–δ bond when rotated less than 180° in a clockwise direction. The values of these torsion angles indicate that the *A* rings have half-chair conformations, the *B* and *C* rings have chair conformations, and the *D* rings have 13β envelope conformations.

The 17β side-chain conformations are illustrated by a Newman projection down the C(17)–C(20) bond as shown in Fig. 3. The average value of the C(13)–C(17)–C(20)–C(21) torsion angle in approximately 40 corticosteroids is 95°, and structures having 17-hydroxy and 21-hydroxy substituents have angles about 10° less

Table 4. *Distance of* O(3) *to the least-squares plane through* C(5) *to* C(17) *inclusive in cortisol and several 9α-halo derivatives*

9α-Chlorocortisol	1·22 Å
Cortisol–methanol	1·32
9α-Bromocortisol	1·37
Cortisol–pyridine	1·77
9α-Fluoro-11β-hydroxy-2α-methylprogesterone	2·03
9α-Fluoro-2α-methylcortisol	2·34
9α-Fluorocortisol	2·43

Table 5. *Intermolecular distances in* (I) *9α-fluoro-2α-methylcortisol and* (II) *9α-fluoro-11β-hydroxy-2α-methylprogesterone*

Contacts which are less than 3·7 Å in either structure are listed.

Atom 1	Atom 2	Position*	Distance (Å) (I)	(II)
C(1)	O(3)	3/−1 1 1	3·90	3·67
C(1)	O(20)	2/ 0 1 0	3·71	3·51
C(3)	O(21)	2/ 0 1 0	3·30	–
C(4)	O(21)	2/ 0 1 0	3·29	–
C(6)	O(21)	1/ 1 0 0	3·59	–
C(7)	C(19)	2/ 1 1 0	3·61	3·74
C(7)	O(21)	1/ 1 0 0	3·64	–
C(11)	O(3)	3/−1 1 1	3·56	3·41
C(11)	O(17)	2/ 0 1−1	3·65	–
C(15)	C(20)	3/ 0 0 1	3·73	3·69
C(15)	O(20)	3/ 0 0 1	3·78	3·57
C(16)	C(21)	3/ 0 0 1	3·67	3·68
C(16)	O(3)	4/ 1−1 1	3·61	3·59
C(16)	O(21)	3/ 0 0 1	3·47	–
C(17)	O(3)	4/ 1−1 1	3·64	3·60
C(20)	F(9)	2/ 0 1−1	3·79	3·61
C(21)	F(9)	2/ 0 1−1	3·65	3·25
C(21)	O(11)	2/ 0 1 0	3·45	3·87
C(22)	O(20)	2/ 0 1 0	3·86	3·63
F(9)	O(20)	2/ 0 1 0	3·53	3·62
F(9)	O(21)	2/ 0 1 0	3·06†	–
O(3)	O(11)	3/ 0 1 1	3·42	2·83†
O(3)	O(17)	4/ 1 0 1	2·75†	–
O(3)	O(21)	2/ 0 1 0	3·57	–
O(11)	O(17)	2/ 0 1−1	2·80†	–

* Symmetry code

1 x, y, z 3 $\frac{1}{2}+x, \frac{1}{2}-y, \bar{z}$

2 $\frac{1}{2}-x, \bar{y}, \frac{1}{2}+z$ 4 $\bar{x}, \frac{1}{2}+y, \frac{1}{2}-z$.

The notation 2/110 means that the second atom is at equivalent position 2, translated one unit cell in the **a** and **b** directions.

† This contact is a hydrogen bond.

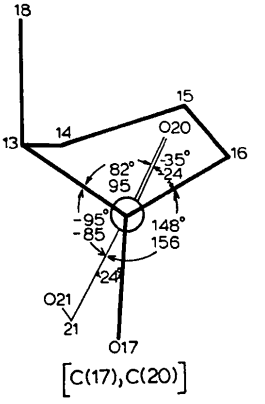

Fig. 3. Newman projection down the C(17)–C(20) bond. Torsion angles for structure (I) are given above those for structure (II).

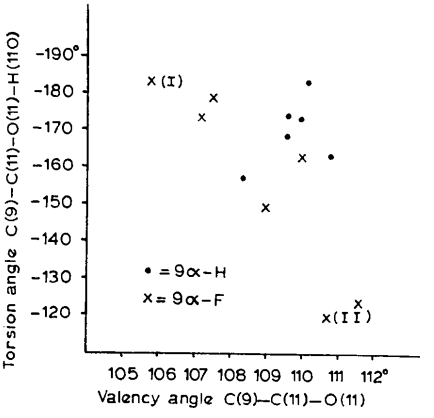

Fig. 4. Correlated variation in the valency angle C(9)–C(11)–O(11) and the torsion angle C(9)–C(11)–O(11)–H(110) in 9α-fluorinated structures.

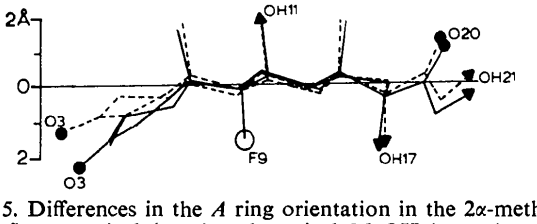

Fig. 5. Differences in the *A* ring orientation in the 2α-methyl-9α-fluorocortisol (——) and cortisol.MeOH (– – – –) structures, visible in a projection parallel to a least-squares plane passed through C(5) to C(17) inclusive.

than structures unsubstituted at these positions (Duax & Norton, 1975). Atoms O(20) and O(21) in structure (I) have the usual *cis* coplanar orientation as indicated by the value of −4·4° for the O(20)–C(20)–C(21)–O(21) torsion angle. Fig. 4 shows the valency angle C(9)–C(11)–O(11) as a function of the position of the O(11) hydroxyl group in those structures for which experimental X-ray positions of H(110) are available. There is little variation in this valency angle in those structures which are unsubstituted at C(9), but there is a correlated variation in the angle C(9)–C(11)–O(11) and the torsion angle C(9)–C(11)–O(11)–H(110) in structures having a 9α-fluoro substituent.

It has been noted previously that the orientation of the *A* ring with respect to the remainder of the nucleus in steroids of the Δ^4-3-one type is subject to considerable variation (Weeks, Duax & Wolff, 1973), and the distance of O(3) to a least-squares plane passing through C(5) to C(17) inclusive (the *BCD* ring plane) provides a convenient quantitative measure of *A* ring orientation. This distance varies from 0·9 to 2·6, with an average value of 1·6 Å, in 20 Δ^4-3-one steroids which are unsubstituted at the 9α-position and which have no additional unsaturation in the *A*, *B* and *C* rings. The larger the distance, the greater the bowing or bending of the molecule towards the α-face.

The *A* ring in 9α-fluorocortisol (Dupont, Dideberg & Campsteyn, 1972) is strongly bowed towards the α-face whereas cortisol as observed in its methanol (Roberts, Coppola, Isaacs & Kennard, 1973) and pyridine (Campsteyn, Dupont & Dideberg, 1974) complexes, 9α-chlorocortisol (Weeks, Duax & Wolff, 1974), and 9α-bromocortisol (Weeks & Duax, 1973) are flatter, as indicated by the O(3) distances in Table 4. The crystal structures of the two 9α-fluoro-2α-methyl steroids reported here were investigated in order to obtain additional observations of the *A*-ring orientation in the presence of a 9α-fluoro substituent, and both molecules are observed to be strongly bowed. The conformational differences between a relatively flat molecule and a bowed molecule are illustrated in Fig. 5, which shows 9α-fluoro-2α-methylcortisol superimposed on the cortisol moiety from the cortisol–methanol structure. These observations suggest that although the *A*-ring orientation in unsubstituted Δ^4-3-one steroids may be relatively flexible in solution, certain substituents such as the 9α-fluoro group may restrict its orientation to a narrower range.

Structures (I) and (II) have similar cell dimensions and similar gross molecular packing. Two views of the packing in structure (I) are given in Fig. 6, and the overall packing of structure (II) appears to be identical in diagrams of this type. However, when the closest intermolecular atomic distances (Table 5) in the two

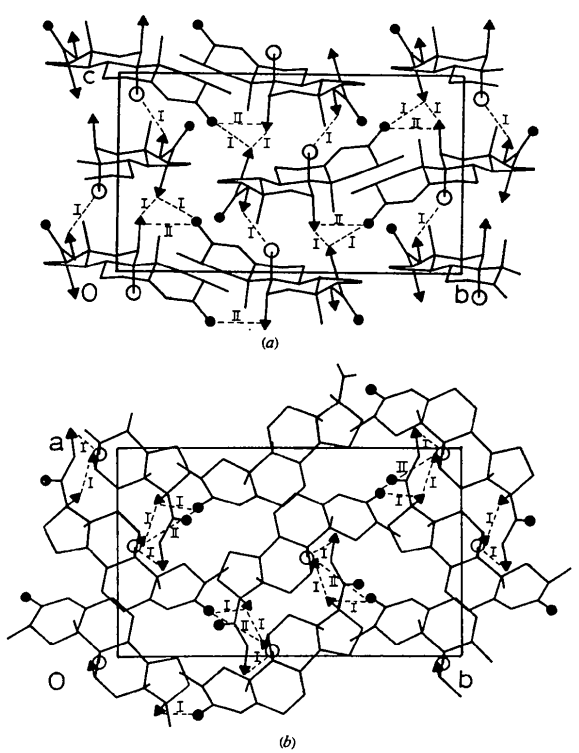

Fig. 6. Molecular packing in structure (I) as seen in projections onto (*a*) the (100) and (*b*) the (001) planes. Hydrogen bonds in both structures are indicated by broken lines and labeled I or II as appropriate. ○ = Fluorine, ● = keto oxygen, and ▲ = hydroxyl oxygen.

Table 6. *Isomorphous steroid crystal structures*

Code No.	Reference	Space group	Cell dimensions a (Å)	b (Å)	c (Å)	β (°)	Number of hydrogen bonds
a_1	(1)	$P2_1$	11·1	8·1	9·6	97·8	3
a_2	(2)	$P2_1$	11·5	8·1	9·4	99·1	3
b_1	(3)	$P2_1$	12·3	7·2	10·3	114·1	2
b_2	(4)	$P2_1$	11·9	7·2	11·0	114·7	2
c_1	(5)	$P2_1$	12·6	7·0	10·9	92·3	0
c_2	(6)	$P2_1$	12·9	7·0	10·6	95·1	0
d_1	(7)	$P2_1$	9·8	14·0	7·8	90·8	0
d_2	(8)	$P2_1$	9·8	12·5	7·3	96·8	0
e_1	(9)	$P2_1$	11·5	11·1	7·6	110·6	0
e_2	(10)	$P2_1$	11·9	11·0	7·8	107·4	2
f_1	(11)	$P2_1$	8·7	12·5	8·5	98·0	0
f_2	(12)	$P2_1$	8·9	12·3	8·3	97·2	1
g_1	(13)	$P2_1$	9·3	22·3	7·6	111·5	2
g_2	(14)	$P2_1$	9·3	23·0	7·6	111·0	6
h_1	(15)	$P2_12_12_1$	10·1	23·6	7·8		3
h_2	(16)	$P2_12_12_1$	10·1	23·7	7·7		2
i_1	(17)	$P2_12_12_1$	13·5	16·6	10·8		1
i_2	(18)	$P2_12_12_1$	13·3	14·5	10·9		0
j_1	(19)	$P2_12_12_1$	10·8	17·6	10·2		3
j_2	(19)	$P2_12_12_1$	10·6	17·0	10·1		1

(1) Busetta, Courseille, Leroy & Hospital, 1972. (2) Busetta, Courseille, Fornies-Marquina & Hospital, 1972. (3) Precigoux, Busetta, Courseille & Hospital, 1972. (4) Weeks, Cooper, Norton, Hauptman & Fisher, 1971. (5) Bordner, Greene, Levine & Sobti, 1973. (6) Sobti, Bordner & Levine, 1971. (7) Duax, Osawa, Cooper & Norton, 1971. (8) Duax, Griffin & Wolff, 1976. (9) Mandel & Donohue, 1972. (10) Ohrt, Cooper & Norton, 1969. (11) Dideberg, Campsteyn & Dupont, 1973. (12) Campsteyn, Dupont, Dideberg & Mandel, 1973. (13) Busetta, Courseille & Hospital, 1973. (14) Cooper, Norton & Hauptman, 1969. (15) Dupont, Dideberg & Campsteyn, 1972. (16) Declercq, Germain & Van Meerssche, 1972. (17) Duax, Eger, Pokrywiecki & Osawa, 1971. (18) Rohrer & Duax, 1975. (19) This work.

structures are compared, several differences, particularly in the hydrogen bonds, are apparent. Structure (I) has three hydrogen donors whereas structure (II) has only one donor. Therefore it is not surprising that structure (I) has more hydrogen bonds, but in view of the gross isomorphism, it is surprising that the single hydrogen bond in structure (II) does not involve the same atoms as any of the hydrogen bonds in structure (I).

On account of the differences in hydrogen-bond patterns in these isomorphous 9α-fluoro-2α-methyl steroids, it is of interest to compare the hydrogen bonds in other isomorphous steroid structures. Nine additional isomorphous pairs were found among the approximately 200 steroids of the estrane, androstane and pregnane type for which atomic coordinates have been reported in the literature, and these structures are listed in Table 6 and drawn schematically in Fig. 7. Only two of these isomorphous pairs (sets *a* and *b*) have identical hydrogen-bond networks. Both members of two pairs (*c* and *d*) and one member of each of three other pairs (*e*, *f* and *i*) have no potential for hydrogen-bond formation. The structures in sets *g* and *h* each have two hydrogen bonds in common, but one member of each pair has additional hydrogen bonds. These differences among the hydrogen bonds in the majority of isomorphous steroid pairs indicate that hydrogen bonds are not of primary importance in determining steroid packing arrangements.

In contrast, there are two examples of true polymorphs (*i.e.* structures in which the composition of the asymmetric unit is the same) among the steroids. The steroid molecules in crystals of estrone I and estrone II (Busetta, Courseille & Hospital, 1973) are related by head-to-tail hydrogen bonding, but in estrone I translationally related molecules are joined whereas molecules related by a screw operation are joined in estrone II. Both of these crystals have space group $P2_12_12_1$. The polymorphs of testosterone monohydrate (Busetta, Courseille, Leroy & Hospital, 1972; Precigoux, Hospital & van den Bosche, 1973) crystallize in space groups $P2_1$ and $P2_12_12_1$ respectively. In both structures there is one hydrogen bond between a water oxygen and an O(3), and there are two hydrogen bonds between water and O(17), giving rise to similar hydrogen-bond networks even though other close intermolecular contacts are different.

This research was supported in part by USPH Research Grant No. CA-10906 from the National Cancer Institute.

References

BORDNER, J., GREENE, R. L., LEVINE, S. G. & SOBTI, R. R. (1973). *Cryst. Struct. Commun.* **2**, 55–58.

BUSETTA, B., COURSEILLE, C., FORNIES-MARQUINA, J. M. & HOSPITAL, M. (1972). *Cryst. Struct. Commun.* **1**, 43–47.

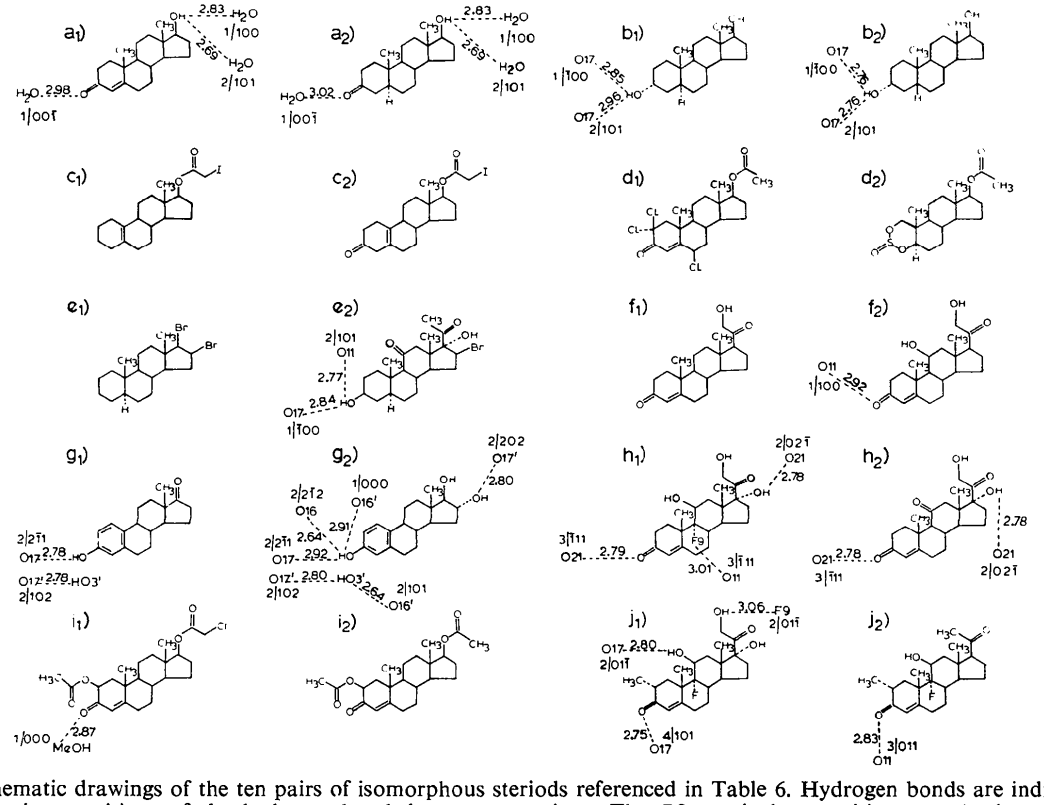

Fig. 7. Schematic drawings of the ten pairs of isomorphous steriods referenced in Table 6. Hydrogen bonds are indicated, and the equivalent positions of the hydrogen-bonded atoms are given. The $P2_1$ equivalent positions are $1=(x,y,z)$ and $2=(\bar{x},\frac{1}{2}+y,\bar{z})$. The $P2_12_12_1$ equivalant positions are defined in the footnote to Table 5.

BUSETTA, B., COURSEILLE, C. & HOSPITAL, M. (1973). *Acta Cryst.* B**29**, 298–313.
BUSETTA, B., COURSEILLE, C., LEROY, F. & HOSPITAL, M. (1972). *Acta Cryst.* B**28**, 3293–3299.
CAMPSTEYN, H., DUPONT, L. & DIDEBERG, O. (1974). *Acta Cryst.* B**30**, 90–94.
CAMPSTEYN, H., DUPONT, L., DIDEBERG, O. & MANDEL, N. (1973). *Acta Cryst.* B**29**, 1726–1728.
COOPER, A., NORTON, D. A. & HAUPTMAN, H. (1969). *Acta Cryst.* B**25**, 814–828.
DECLERCQ, J. P., GERMAIN, G. & VAN MEERSSCHE, M. (1972). *Cryst. Struct. Commun.* **1**, 13–15.
DIDEBERG, O., CAMPSTEYN, H. & DUPONT, L. (1973). *Acta Cryst.* B**29**, 103–112.
DUAX, W. L., EGER, C., POKRYWIECKI, S. & OSAWA, Y. (1971). *J. Med. Chem.* **14**, 295–300.
DUAX, W. L., GRIFFIN, J. F. & WOLFF, M. E. (1976). *Cryst. Struct. Commun.* **5**, 279–282.
DUAX, W. L. & NORTON, D. A. (1975). *Atlas of Steroid Structure.* New York: Plenum.
DUAX, W. L., OSAWA, Y., COOPER, A. & NORTON, D. A. (1971). *Tetrahedron*, **27**, 331–335.
DUPONT, L., DIDEBERG, O. & CAMPSTEYN, H. (1972). *Acta Cryst.* B**28**, 3023–3032.
GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.
HOGG, J. A., LINCOLN, F. H., JACKSON, R. W. & SCHNEIDER, W. P. (1955). *J. Amer. Chem. Soc.* **77**, 6401.
MANDEL, N. & DONOHUE, J. (1972). *Acta Cryst.* B**28**, 308–312.
OHRT, J. M., COOPER, A. & NORTON, D. A. (1969). *Acta Cryst.* B**25**, 41–51.
PRECIGOUX, G., BUSETTA, B., COURSEILLE, C. & HOSPITAL, M. (1972). *Cryst. Struct. Commun.* **1**, 265–268.
PRECIGOUX, G., HOSPITAL, M. & VAN DEN BOSCHE, G. (1973). *Cryst. Struct. Commun.* **3**, 435–439.
ROBERTS, P. J., COPPOLA, J. C., ISAACS, N. W. & KENNARD, O. (1973). *J. Chem. Soc. Perkin* II, pp. 774–781.
ROHRER, D. C. & DUAX, W. L. (1975). *Cryst. Struct. Commun.* **4**, 265–269.
SOBTI, R. R., BORDNER, J. & LEVINE, S. F. (1971). *J. Amer. Chem. Soc.* **93**, 5588–5590.
STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination.* New York: Macmillan.
WEEKS, C. M., COOPER, A., NORTON, D. A., HAUPTMAN, H. & FISHER, J. (1971). *Acta Cryst.* B**27**, 1562–1572.
WEEKS, C. M. & DUAX, W. L. (1973). *Acta Cryst.* B**29**, 2210–2213.
WEEKS, C. M., DUAX, W. L. & WOLFF, M. E. (1973). *J. Amer. Chem. Soc.* **95**, 2865–2868.
WEEKS, C. M., DUAX, W. L. & WOLFF, M. E. (1974). *Acta Cryst.* B**30**, 2516–2519.

Acta Cryst. (1976). B**32**, 2825

The Crystal Structure of the Cubic Cadmium Phosphorus Sulphide Iodide $Cd_{13}P_4S_{22}I_2$

BY A. BUBENZER, R. NITSCHE AND E. GRIESHABER

Kristallographisches Institut der Universität, D-7800 Freiburg/Breisgau, Hebelstr. 25, Germany (BRD)

(*Received* 17 *March* 1976; *accepted* 23 *April* 1976)

Crystals of $Cd_{13}P_4S_{22}I_2$ have been grown by vapour transport. They are cubic, space group $F\bar{4}3m$; $a=9{\cdot}969$ (1) Å; $Z=1$. The intensities were measured on a Nonius CAD-4 diffractometer. A Patterson synthesis revealed the basic structure. A least-squares refinement, taking into account anisotropic temperature factors, isotropic extinction and anomalous scattering for the Cd atoms, led to a final R of 0·065. The structure consists of a framework of interpenetrating S–I icosahedra, forming a tetrahedrally close-packed anion sublattice which is closely related to the Laves phase $MgCu_2$. The P atoms are exactly tetrahedrally coordinated by four S atoms. The Cd atoms occupy two different positions: Cd(1) is situated in a distorted tetrahedron consisting of two S and two '(S,I) atoms', *i.e.* positions containing S and I in a statistical distribution. Cd(2) is in triangular coordination by three anions.

Introduction

In the system Cd–P–S only one compound, cadmium hypothiosulphate $Cd_2[P_2S_6]$ (with formally tetravalent P), has been reported (Klingen, Ott & Hahn, 1973; Klingen, Eulenberger & Hahn, 1973). Recently, we have found (Nitsche, Grieshaber & Bubenzer, 1976) that another compound, $Cd_{14}P_4S_{24}$ (with pentavalent P), exists. It is monoclinic ($Z=1$) and X-ray data indicate that its structure is nearly identical to the also monoclinic (space group Cc) structure of $Cd_{16}Ge_4S_{24}$ (Nitsche, 1964; Susa & Steinfink, 1971) and to the isomorphous $Cd_{16}Si_4S_{24}$ (Krebs & Mandt, 1972). Furthermore, we have found that a closely related cubic structure can be obtained if one replaces two S atoms of the anion sublattice of $Cd_{14}P_4S_{24}$ by two I atoms. The resulting compound, $Cd_{13}P_4S_{22}I_2$, contains, for electrochemical neutrality, only 13 Cd atoms.

Crystals of $Cd_{13}P_4S_{22}I_2$ (bright yellow tetrahedra up to $2\times2\times2$ mm) are obtained by reacting the elements