Acta Cryst. (1973). B29, 199

The Molecular Structure of 17-Hydroxyprogesterone 17-(10-Chloro-9-ketodecanoate) and 17-Hydroxyprogesterone 17-(10-Hydroxy-9-ketodecanoate)*

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(*Received* 29 *June* 1972; *accepted* 12 *October* 1972)

The steroid ester 17-hydroxyprogesterone 17-(10-chloro-9-ketodecanoate), $C_{31}H_{45}O_5Cl$, is a potent irreversible inhibitor of corticosteroid acetyltransferase while its analog, 17-hydroxyprogesterone 17-(10-hydroxy-9-ketodecanoate), $C_{31}H_{46}O_6$, is not a good substrate. The structures of the two steroids were determined from room-temperature counter-collected X-ray data through the application of direct methods. The space group for both compounds is $P2_1$ with cell dimensions of $a=14{\cdot}505$ (3), $b=7{\cdot}668$ (2), $c=13{\cdot}511$ (3) Å and $\beta=107{\cdot}97$ (2)° for the chloro derivative and $a=14{\cdot}066$ (9), $b=7{\cdot}666$ (3), $c=13{\cdot}493$ (5) Å and $\beta=106{\cdot}03°$ for the hydroxy compound. The observed densities are $d_{Cl}=1{\cdot}234$ and $d_{OH}=1{\cdot}202$ g.cm^{-3}, which are consistent with two molecules per unit cell and calculated densities $d_{Cl}=1{\cdot}235$ and $d_{OH}=1{\cdot}215$ g.cm^{-3}. 3189 independent reflections were collected for the chloro derivate and 2667 for the hydroxy. The model of the chloro derivative was refined by conventional least-squares techniques to an R index of 0·069 while refinement of the hydroxy derivative was terminated at $R=0{\cdot}135$. The conformations of the extended side chains are the same within experimental error except for the position of the terminal chloro and hydroxy groups. There are no significant intramolecular interactions.

Introduction

Corticosteroid acetyltransferase (CoAc), a soluble enzyme isolated from the major anatomical areas of the primate brain (Purdy, Grossner & Axelrod, 1968), catalyzes the formation of 21-hydroxysteroid esters, principally acetates, in the presence of acyl coenzyme A derivatives. The mechanism of this reaction, using acetyl CoA as coenzyme, involves the initial formation of an acetyl-enzyme intermediate, with the subsequent transfer of the acetyl group to the 21-alcohol group of the steroid substrate (Purdy, 1971). Amongst naturally occurring compounds, only primary 21-hydroxy 20-ketosteroids serve as substrates. A study of a number of 16α-hydroxysteroids demonstrated that they are very poor substrates and act as competitive inhibitors (Purdy & Rao, 1970). A similar result is found for the 16α-methylcorticoid, dexamethasone (Purdy, 1972). These observations prompted further studies of ring *D* substituted compounds to elucidate the nature of the interaction of CoAc with steroidal derivatives.

The compound 17-hydroxyprogesterone 17-(10-chloro-9-ketodecanoate) is a potent irreversible inhibitor of CoAc but the primary α-ketol analog 17-hydroxyprogesterone 17-(10-hydroxy-9-ketodecanoate) is not a substrate (Purdy & Rao, 1969). In contrast to the above results, 21-chloro-17-hydroxyprogesterone is also a potent irreversible inhibitor and the analogous 17,21-dihydroxyprogesterone is a good substrate of CoAc. This similar behavior of the chloromethylketones and dissimilar behavior of the α-ketols led to a postulation of differences in conformation or stereochemical configuration between the two progesterone 17-esters. It was inferred that the chlorine atom might be close to the position of the C(21) methyl group while the side chain of the hydroxy compound existed in an extended conformation.

Differences in configuration could be determined by an X-ray analysis. Differences in conformation might be significant if strong intramolecular interactions are also present in aqueous solution. If the two progesterone 17-esters have identical conformations in the solid state, differences may still exist in solution. However, different modes of binding for the two types of substrates and inhibitors or the alkylation of different amino acid residues of the enzyme by the two chloromethylketone inhibitors become viable alternatives. In order to assist elucidation of the mechanism of this enzyme we have determined the structures of the two progesterone 17-esters.

These X-ray analyses also indicate a possible conformation for the widely employed progestational agent, 17-hydroxyprogesterone-17-(n-caproate). The parent compound, 17-hydroxyprogesterone, has no apparent hormonal effects in man. However the caproate ester a has marked and prolonged progestational activity *in vivo* where it apparently does not undergo hy-

* Contribution number 9 from the Fastbios Laboratory.

drolysis (Reifenstein, 1957). It has been concluded that straight-chain esters of 17-hydroxyprogesterone, containing eight or more contiguous carbon atoms in the acid moiety, have an increased association with the biological receptor(s) that control their hormonal activity (Solo & Gardner, 1971).

Experimental

Samples of the 10-chloro and 10-hydroxy-9-ketodecanoate compounds contained small crystals and those of the 10-hydroxy compound were not suitable for accurate X-ray analysis. The small amount of sample prevented extensive variations in recrystallization techniques. The cell dimensions and estimated standard deviations of each compound were obtained from a least-squares treatment of 65 high order, general reflections collected on a General Electric XRD-6 diffractometer. The densities were determined by the flotation technique using a mixture of cyclohexane and carbon tetrachloride. The intensities were measured by the stationary-crystal stationary-counter method (Furnas & Harker, 1955). Ni–Co balanced Ross filters and electronic pulse height discrimination were used for monochromatization.

17-*hydroxyprogesterone* 17-(10-*chloro*-9-*ketodecanoate*, $C_{31}H_{45}O_5Cl$, M. W. 532.
$a=14{\cdot}505$ (3), $b=7{\cdot}668$ (2), $c=13{\cdot}511$ (3) Å; $\beta=107{\cdot}97$ (2)°. Systematic absences: $0k0$, $k=2n+1$. Space group: $P2_1(C_2^2$, No. 4); $Z=2$; $F(000)=576$; $V=1429$ Å^3; $\mu=14{\cdot}89$ cm^{-1} (Cu $K\alpha$); $D_{exp}=1{\cdot}234$ g.cm^{-3}; $D_{cal}=1{\cdot}235$ g.cm^{-3}; Cu $K\alpha=1{\cdot}54178$ Å.

A crystal of dimensions $0{\cdot}089\times0{\cdot}232\times1{\cdot}143$ mm was used for all intensity measurements. The crystal was mounted with the long axis (b) coincident with the fiber axis. 3189 reflections were measured ($2\theta<110°$) of which 3135 were considered to be observed, $2\sigma(F)<F_o$. Lorentz–polarization factors were applied and the data were processed in the usual way. The data were corrected automatically for absorption although differences in maximum and minimum transmission factors were negligible.

17-*hydroxyprogesterone* 17-(10-*hydroxy*-9-*ketodecanoate*), $C_{31}H_{46}O_6$. M. W. 514.
$a=14{\cdot}066$ (9), $b=7{\cdot}666$ (3), $c=13{\cdot}493$ (5) Å; $\beta=106{\cdot}03$ (6)°; $V=1398$ Å^3; $F(000)=560$; $\mu=6{\cdot}70$ cm^{-1}; $D_{exp}=1{\cdot}202$ g cm^{-3}; $D_{cal}=1{\cdot}215$ g cm^{-3}.

A crystal of dimensions $0{\cdot}039\times0{\cdot}116\times0{\cdot}603$ mm was used for all intensity measurements. The crystal was mounted with the long axis (b) coincident with the fiber axis. 2859 independent reflections were collected on a General Electric XRD 490 diffractometer of which 2667 were considered to be observed. In addition, 1825 independent reflections were collected on a Phillips PAILRED diffractometer of which 848 were considered to be observed. Six levels were collected along the b axis with an ω-scan rate of 1° per min and a background count of 10 sec at each end of the scan range. Lorentz–polarization corrections were applied to the two sets of data, and the intensities were averaged to give one set of 2667 independent reflections.

The data on the two compounds were adjusted to an absolute scale by Wilson plots. Standard deviations were assigned to each reflection on the basis of counting statistics and the weighting factor $w=[1/\sigma(F_o)]^2$ was used in all calculations. In addition to the structure-factor magnitudes $|F_o|$ the normalized structure factor magnitudes $|E_h|$ were computed. The scattering factors of Cromer & Waber (1965) were used for all heavy atoms and those of Stewart, Davidson & Simpson (1965) were used for the hydrogen atoms. The scattering factors for the chlorine atom were corrected for the real and imaginary parts of the anomalous dispersion (Cromer, 1965).

Structure determination and refinement

The structure was solved by application of the symbolic addition technique, tangent refinement, successive electron-density calculations and least-squares refinement. The program *PHASE*, used in the first part of the analysis, was written for the CDC 6600 by Koenig (1969) and modified for the IBM 1800 as part of the Fastbios Laboratory program package (Stemple, 1970).

The data from the 10-hydroxy derivative initially were used to solve the structure. Three origin defining reflections (709, $\bar{4}07$, 10,1,2) were selected on the basis of their magnitudes, number of contributions, and the requirement of linear independence (Hauptman & Karle, 1956). Four additional reflections, (10,0,8, 918, 133, 239), were selected and assigned the symbolic phases a, b, c and d. Four cycles of symbolic addition (Karle & Karle, 1964, 1966) phased 72 reflections from the set of $155E$'s $>1{\cdot}80$. Relationships were derived between a, b, c and d, and one cycle of tangent refinement (Karle & Hauptman, 1956) with the $155E$'s $>1{\cdot}80$ phased 124 reflections. A second cycle with the $661E$'s $>1{\cdot}20$ phased 509 reflections. An E map calculated with the 509 phased reflections revealed the positions of 22 atoms and one least-squares cycle of refinement gave an R index of 0·28 where $R=\sum||F_o|-|F_c||/\sum|F_o|$. The phases from this refinement were used in one additional cycle of tangent refinement and 520 reflections were phased. A second E map calculated with these phases revealed the positions of 37 atoms, and two cycles of isotropic least-squares refinement gave an R index of 0·17. Several cycles of anisotropic refinement reduced R to 0·135. Because of the poor quality of the 10-hydroxy crystals a detailed refinement was made with the data obtained from the 10-chloro derivative.

The atomic parameters found for the 10-hydroxy compound were used in a least-squares refinement of the data for the 10-chloro derivative. Ten cycles

of isotropic block-diagonal least-squares refinement yielded $R=0{\cdot}111$ for 1190 of the strongest reflections. The function minimized was $\sum w(F_o-F_c)^2$. Six cycles of anisotropic block-diagonal refinement (5 blocks) yielded $R=0{\cdot}095$ for 1713 of the strongest reflections. All non-methyl hydrogen atom positions were calculated and their contributions to the structure factors in the final cycle of refinement were computed but their positions were not refined. Peaks consistent with methyl hydrogen positions were observed in a difference Fourier map and these positions are listed in Table 2, however, some rotation of the methyl groups is expected. A final cycle of refinement reduced the R index to 0·069. Bond distances appeared reasonable, and the refinement was terminated at this point. A structure factor calculation with all 3189 reflections gave R index of 0·099. IBM 1800, 360/50 and 360/65 computers were used in the refinement.

A three-dimensional difference Fourier map indicated no peak larger than a hydrogen atom. The standard deviations were estimated from the inverses of the blocks from the last least-squares cycle. Previous studies in this laboratory indicate that these deviations should be multiplied by a factor of approximately 1·2. A table listing the squares of the observed and calculated structure factors has been deposited with the National Lending Library, England, as Supplementary Publication No. SUP 30024.* Atomic and thermal parameters are listed in Table 1. The structures of the two steroids are the same within experimental error except for a small shift in the positions of the chloro and hydroxy groups. The parameters of the oxygen atom in the 10-hydroxy compound are listed at the end of Table 1.

* Copies of this table may be obtained through the Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1. *Atomic and thermal parameters for* 17-*hydroxyprogesterone* 17-(10-*chloro*-9-*ketodecanoate*)

Thermal parameters are of the form $\exp[-\frac{1}{4}(B_{11}h^2a^{*2}+B_{22}k^2b^{*2}+B_{33}l^2c^{*2}+2B_{12}hka^*b^*+2B_{13}hla^*c^*+2B_{23}klb^*c^*)]$. Coordinates are $\times 10^4$ except for hydrogen for which they are $\times 10^3$.

	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Cl	−858 (2)	7923 (7)	6239 (3)	7·3 (2)	9·2 (3)	15·5 (3)	3·3 (2)	3·6 (2)	0·6 (2)
O(1)	4353 (4)	3105 (12)	1918 (5)	5·3 (2)	7·6 (4)	5·1 (3)	−0·5 (3)	−0·4 (2)	0·6 (3)
O(2)	9530 (4)	1866 (11)	542 (5)	4·6 (2)	7·3 (4)	5·4 (3)	0·0 (3)	−1·3 (2)	−0·3 (3)
O(3)	7051 (3)	1940 (8)	9218 (4)	3·3 (2)	4·7 (3)	3·4 (2)	0·2 (2)	0·8 (1)	0·1 (2)
O(4)	7397 (4)	2066 (11)	946 (4)	5·1 (2)	7·6 (4)	3·4 (2)	−0·1 (3)	−0·1 (2)	0·2 (3)
O(5)	−183 (6)	4456 (17)	5817 (8)	6·9 (4)	9·4 (7)	12·6 (6)	1·8 (5)	−2·3 (4)	−2·6 (6)
C(1)	6176 (6)	1200 (13)	4122 (6)	4·6 (4)	4·4 (4)	3·6 (3)	0·3 (3)	0·2 (3)	−0·1 (3)
C(2)	5707 (7)	1466 (15)	2944 (6)	6·5 (5)	5·1 (5)	3·5 (3)	−0·3 (4)	0·6 (3)	−0·3 (3)
C(3)	5049 (6)	2997 (14)	2725 (6)	5·5 (4)	5·0 (5)	3·5 (3)	−0·2 (4)	1·1 (3)	0·8 (4)
C(4)	5316 (6)	4454 (14)	3454 (6)	5·7 (4)	4·5 (4)	3·7 (3)	0·8 (4)	0·9 (3)	0·4 (3)
C(5)	6087 (5)	4428 (13)	4303 (6)	4·0 (3)	4·0 (4)	3·9 (3)	−0·0 (3)	1·2 (3)	0·2 (3)
C(6)	6400 (7)	6070 (13)	4922 (7)	5·6 (4)	3·8 (4)	4·9 (4)	−0·0 (4)	0·2 (3)	0·4 (4)
C(7)	6601 (6)	5789 (12)	6092 (6)	5·2 (4)	3·4 (4)	4·1 (3)	0·4 (4)	0·0 (3)	0·0 (3)
C(8)	7293 (6)	4281 (12)	6490 (6)	4·2 (3)	3·1 (4)	3·7 (3)	−0·5 (3)	1·1 (3)	−0·0 (3)
C(9)	6843 (5)	2612 (11)	5864 (5)	3·5 (2)	3·0 (3)	3·4 (3)	0·2 (3)	1·0 (2)	0·1 (3)
C(10)	6691 (5)	2836 (12)	4654 (5)	3·4 (3)	4·2 (4)	3·1 (3)	−0·0 (3)	0·6 (2)	−0·1 (3)
C(11)	7461 (6)	983 (11)	6323 (6)	5·9 (4)	2·5 (4)	3·6 (3)	0·4 (3)	1·1 (3)	0·0 (3)
C(12)	7598 (6)	715 (12)	7496 (6)	4·4 (3)	3·1 (4)	3·8 (3)	0·1 (3)	0·5 (3)	−0·3 (3)
C(13)	8030 (5)	2356 (12)	8111 (6)	2·7 (2)	3·7 (3)	3·7 (3)	−0·0 (3)	0·4 (2)	0·1 (3)
C(14)	7395 (5)	3947 (11)	7646 (6)	3·9 (3)	3·0 (4)	3·8 (3)	−0·0 (3)	0·6 (3)	0·2 (3)
C(15)	7792 (7)	5414 (13)	8431 (7)	5·7 (4)	3·6 (4)	4·4 (3)	−0·8 (4)	0·2 (3)	−0·6 (3)
C(16)	8122 (6)	4427 (14)	9474 (6)	5·3 (4)	4·1 (4)	3·9 (3)	−0·6 (4)	0·5 (3)	−0·5 (3)
C(17)	7997 (5)	2495 (12)	9249 (6)	3·3 (3)	3·9 (4)	3·8 (3)	0·5 (3)	0·1 (3)	−0·5 (3)
C(18)	9092 (5)	2575 (15)	8087 (6)	3·8 (3)	5·8 (5)	4·4 (3)	0·3 (4)	0·7 (3)	−0·1 (4)
C(19)	7664 (6)	3057 (16)	4430 (7)	5·2 (4)	6·5 (6)	4·2 (3)	0·7 (4)	1·6 (3)	0·4 (4)
C(20)	8759 (6)	1296 (15)	9997 (6)	4·1 (3)	6·8 (6)	3·3 (3)	1·0 (4)	0·5 (3)	0·0 (4)
C(21)	8548 (7)	−638 (15)	9944 (7)	5·7 (4)	4·6 (5)	4·5 (3)	0·8 (4)	0·8 (3)	0·3 (4)
C(22)	6825 (6)	1801 (13)	109 (6)	5·1 (4)	4·2 (4)	4·2 (3)	0·3 (4)	1·6 (3)	0·0 (3)
C(23)	5795 (6)	1259 (14)	9900 (6)	5·1 (4)	5·1 (5)	4·6 (3)	0·4 (4)	1·6 (3)	0·8 (4)
C(24)	5035 (5)	2134 (14)	8995 (6)	3·3 (3)	5·2 (5)	4·2 (3)	0·1 (3)	0·6 (3)	0·2 (4)
C(25)	4016 (7)	1493 (14)	8857 (7)	5·5 (4)	4·4 (4)	4·7 (3)	0·4 (4)	1·4 (3)	0·1 (4)
C(26)	3252 (5)	2389 (15)	7953 (7)	3·4 (3)	6·2 (6)	5·5 (4)	0·1 (4)	1·3 (3)	0·6 (4)
C(27)	2250 (7)	1632 (16)	7805 (8)	5·0 (4)	5·0 (5)	6·6 (5)	−0·4 (4)	1·3 (4)	−0·9 (4)
C(28)	1439 (7)	2478 (17)	6900 (8)	4·4 (4)	6·2 (6)	7·4 (5)	0·7 (4)	0·3 (4)	−1·9 (5)
C(29)	1313 (8)	4401 (18)	7082 (8)	6·2 (5)	5·9 (6)	5·4 (4)	−0·0 (5)	−0·1 (4)	0·0 (5)
C(30)	414 (7)	5231 (18)	6473 (9)	3·1 (4)	7·6 (7)	6·8 (5)	0·3 (4)	1·4 (4)	−0·0 (5)
C(31)	327 (7)	7113 (19)	6716 (10)	4·8 (5)	7·2 (8)	10·2 (7)	0·6 (5)	1·9 (5)	−0·6 (7)
O[1]	−796	8054	5990	5·4	10·9	9·9	5·7	2·5	3·5

[1] Position of the hydroxyl oxygen in 17-hydroxyprogesterone 17-(10-hydroxy-9-ketodecanoate).

Table 1 (*cont.*)

	x	*y*	*z*	*B*
H(C1*A*)	670	14	425	2·0
H(C1*B*)	566	79	450	2·0
H(C2*A*)	624	158	255	2·0
H(C2*B*)	529	27	264	2·0
H(C4)	485	567	325	2·0
H(C6*A*)	703	662	478	2·0
H(C6*B*)	585	708	465	2·0
H(C7*A*)	689	699	651	2·0
H(C7*B*)	591	554	627	2·0
H(C8)	799	461	641	2·0
H(C9)	616	253	600	2·0
H(C11*A*)	817	110	618	2·0
H(C11*B*)	716	−15	589	2·0
H(C12*A*)	809	−36	774	2·0
H(C12*B*)	693	41	758	2·0
H(C14)	668	376	773	2·0
H(C15*A*)	837	605	829	2·0
H(C15*B*)	719	625	847	2·0
H(C16*A*)	889	470	983	2·0
H(C16*B*)	770	480	998	2·0
H(C18*A*)	941	373	852	2·0
H(C18*B*)	947	137	831	2·0
H(C18*C*)	909	289	730	2·0
H(C19*A*)	758	301	361	2·0
H(C19*B*)	819	210	482	2·0
H(C19*C*)	797	436	471	2·0
H(C21*A*)	903	−126	63	2·0
H(C21*B*)	866	−120	926	2·0
H(C21*C*)	781	−87	993	2·0
H(C23*A*)	573	−11	982	2·0
H(C23*B*)	558	148	60	2·0
H(C24*A*)	522	190	827	2·0
H(C24*B*)	506	357	909	2·0
H(C25*A*)	399	8	874	2·0
H(C25*B*)	383	174	959	2·0
H(C26*A*)	345	223	724	2·0
H(C26*B*)	323	379	810	2·0
H(C27*A*)	225	23	766	2·0
H(C27*B*)	203	177	849	2·0
H(C28*A*)	164	234	616	2·0
H(C28*B*)	76	180	675	2·0
H(C29*A*)	191	517	697	2·0
H(C29*B*)	142	463	789	2·0
H(C31*A*)	82	786	645	2·0
H(C31*B*)	57	726	758	2·0

Discussion

Fig. 1 shows a projection of the unit-cell contents onto the *ac* plane, and Fig. 2 gives bond lengths and angles. The corrected average standard deviation for the distances is approximately 0·01 Å and that for the angles is 0·9°. Table 2 gives the least-squares planes through selected atoms and Table 3 lists selected interplanar angles.

Table 3. *Interplanar angles*

Plane 1	Plane 2	Angle
*A*1	*A*2	160°
*A*3*B*1	*A*2	150
*A*3*B*1	*B*2	122
*B*3*C*1	*B*2	128
*B*3*C*1	*C*2	126
*C*3*D*1	*C*2	130
*C*3*D*1	*D*2	132
*C*3*D*1	*D*3	146
A	*B*	159
B	*C*	164
C	*D*	163

Steroid nucleus

The *A*, *B* and *C* rings exhibit the chair conformation while the *D* ring is a distorted half chair with $\Delta = 23°$ and $\varphi_0 = 47·7$ (Altona, Geise & Romers, 1968). The bond lengths are consistent with those observed in similar steroids (Cooper & Norton, 1968*a*, *b*; Cooper, Lu & Norton, 1968; Duax, Cooper & Norton, 1971). A least-squares plane fitted to the steroid nucleus shows an average deviation of 0·25 Å with C(3), C(4), C(8), C(10), and C(17) lying approximately 0·5 Å out of the plane. A least-squares plane fitted to atoms C(2)O(3)C(4)C(5)C(6) and C(10), which comprise the Δ^4-3-one system and its neighbors, has an average deviation of 0·07 Å with atoms C(2), C(6) and C(10) out of the plane by more than 0·10 Å. Torsion angles within the steroid nucleus (Klyne & Prelog, 1960) are listed in Table 4.

Table 2. *Least-squares planes through selected atoms*

The equations are of the form $ax+by+cz=d$ where *y* is coincident with the *b* axis, *x* is coincident with the *a* axis and *z* is perpendicular to *x* and *y*.

Plane	Atoms	*a*	*b*	*c*	*d*	Avg. dev
*A*1	C(2)C(3)C(4)	0·7274	0·4038	−0·5547	3·5188	—
*A*2	C(1)C(2)C(4)C(5)	0·9180	0·2450	−0·3118	5·4550	0·17
*A*3*B*1	C(1)C(5)C(6)C(10)	0·5674	−0·1371	0·8119	8·5519	0·32
*B*2	C(6)C(7)C(9)C(10)	0·9724	0·1712	0·1586	8·9569	0·02
*B*3*C*1	C(7)C(8)C(9)C(11)	0·6046	0·1677	0·7786	11·3737	0·35
*C*2	C(8)C(11)C(12)C(14)	0·9726	0·1120	0·2037	9·8540	0·01
*C*3*D*1	C(12)C(13)C(14)C(15)	0·4104	−0·1830	0·8933	12·0135	0·36
*D*2	C(13)C(15)C(16)C(17)	0·9781	0·0938	0·1856	10·2961	0·11
*D*3	C(14)C(15)C(16)C(17)	0·9889	−0·0689	−0·1312	6·1327	0·03
A	C(1)C(2)C(3)C(4)C(5)C(10)	0·8487	0·2593	−0·4608	4·3170	0·15
B	C(5)C(6)C(7)C(8)C(9)C(10)	0·9710	0·2144	−0·1056	7·2810	0·22
C	C(8)C(9)C(11)C(12)C(13)C(14)	0·9481	0·1357	−0·1147	7·1160	0·24
D	C(13)C(14)C(15)C(16)C(17)	0·9917	0·1257	−0·0281	7·9957	0·19
ABCD	C(1)–C(17)	0·9712	0·1662	−0·1706	6·4510	0·26
*A*4*B*4	C(2)C(3)C(4)C(5)C(6)C(10)O(1)	0·7804	0·3297	−0·5311	3·7789	0·07

Table 4. *Torsion angles in the rings and side chain*

Ring *A*		Ring *B*		Ring *C*		Ring *D*	
Bond	(*A*–*B*)	Bond	(*A*–*B*)	Bond	(*A*–*B*)	Bond	(*A*–*B*)
C(1)–C(2)	−54·5°	C(5)–C(6)	−49·6°	C(8)—C(9)	−54·9°	C(13)–C(14)	+46·7°
C(2)–C(3)	+32·6	C(6)–C(7)	+52·1	C(9)—C(11)	+55·6	C(14)–C(15)	−32·6
C(3)–C(4)	−2·4	C(7)–C(8)	−57·2	C(11)–C(12)	−55·5	C(15)–C(16)	+5·2
C(4)–C(5)	+6·9	C(8)–C(9)	+60·5	C(12)–C(13)	+54·7	C(16)–C(17)	+23·8
C(5)–C(10)	−15·3	C(9)–C(10)	−55·8	C(13)–C(14)	−59·3	C(13)–C(17)	−42·9
C(1)–C(10)	+68·5	C(5)–C(10)	50·0	C(8)—C(14)	+58·9		

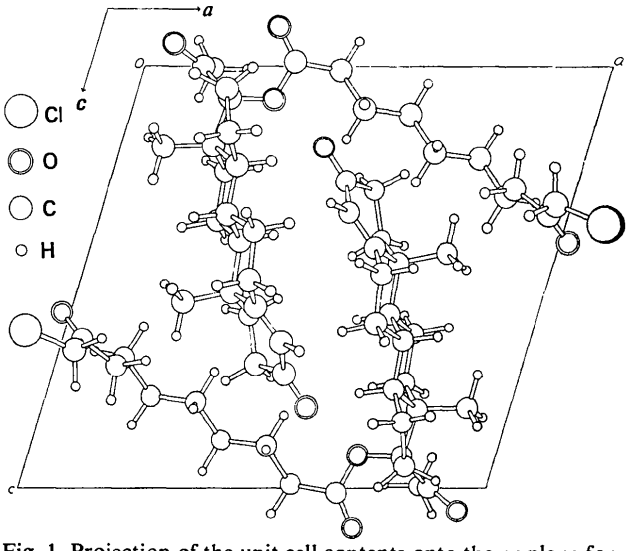

Fig. 1. Projection of the unit cell contents onto the *ac* plane for 17-hydroxyprogesterone 17-(10-chloro-9-ketodecanoate).

Table 4 (*cont.*)

$\chi(1)$ = C(17)O(3)C(22)C(23)	+178
$\chi(2)$ = O(3)C(22)C(23)C(24)	−43
$\chi(3)$ = C(22)C(23)C(24)C(25)	+179
$\chi(4)$ = C(23)C(24)C(25)C(26)	+179
$\chi(5)$ = C(24)C(25)C(26)C(27)	−177
$\chi(6)$ = C(25)C(26)C(27)C(28)	−179
$\chi(7)$ = C(26)C(27)C(28)C(29)	−62
$\chi(8)$ = C(27)C(28)C(29)C(30)	−162
$\chi(9)$ = C(28)C(29)C(30)C(31)	−178

Side chains

The conformations about the C(17)–C(20), C(17)–O(3), and C(31)–C(30) bonds are shown in Fig. 3 while the torsion angles for C(17) through C(31) (Edsall *et al.*, 1966) are listed in Table 4. The conformation of the C(17) keto side chain is similar to that found for other steroids (Duax, Cooper & Norton, 1971). The chlorine atom and oxygen atom O(5) associated with the C(31)–C(30) bond are almost eclipsed although this would appear to be both sterically and electrostatically unfavorable. The C–Cl distance of 1·763 Å

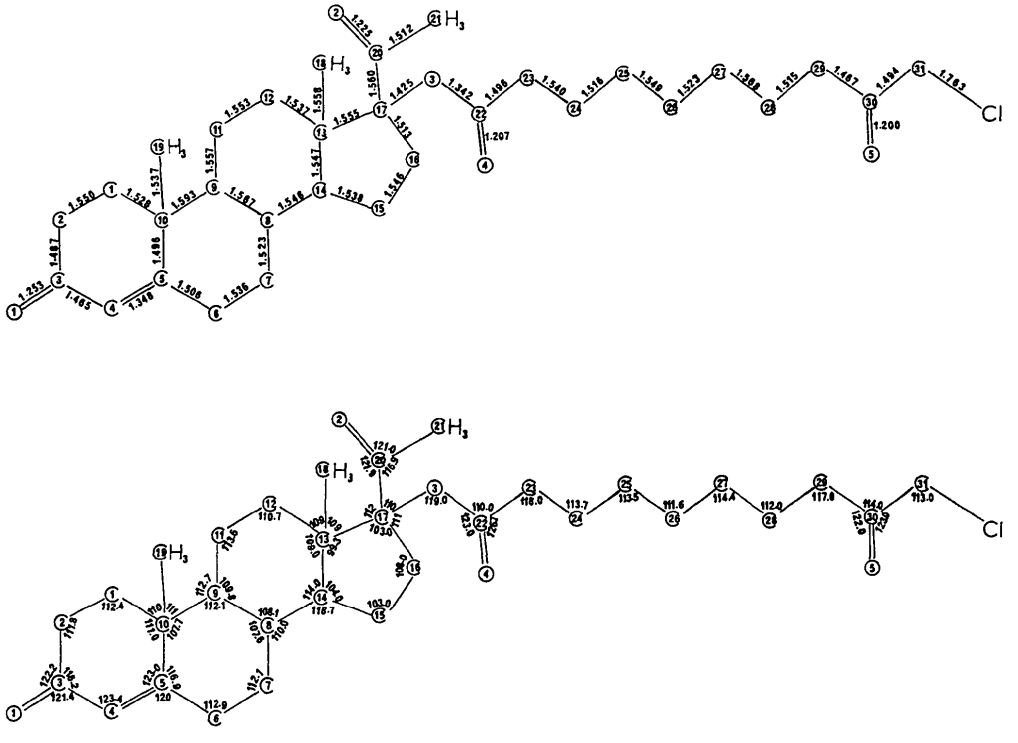

Fig. 2. Bond lengths and bond angles for 17-hydroxyprogesterone 17-(10-chloro-9-ketodecanoate).

is consistent with carbon–chlorine bonds found in a variety of compounds. Large anisotropic thermal motions are associated with the terminal atoms of the decanoate chain; however, the thermal motions of the remainder of the atoms are normal. The long side chain is extended away from the steroid nucleus and there are no intramolecular interactions in the solid state between the side chain and the steroid nucleus.

We would like to express our appreciation to the Robert A. Welch Foundation for their financial support and the TCU Research Foundation for the equipment. The study was also assisted in part by Grant NSO9915 from the National Institute of Neurological Diseases and Stroke to R. H. P.

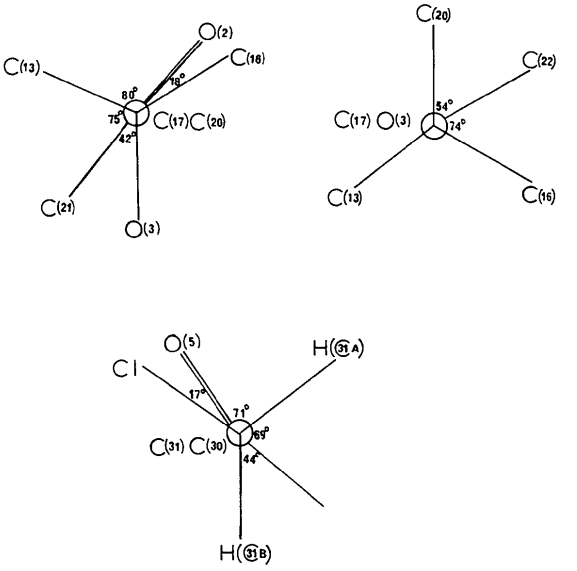

Fig. 3. Conformations about selected bonds in 17-hydroxyprogesterone 17-(10-chloro-9-ketodecanoate).

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