# Crystalline Molecular Structures of Two Derivatives of 2β-Hydroxytestosterone Having an Unusual A-Ring Conformation

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In the crystal structures of 2β-acetoxy-17β-chloroacetoxy-4-androsten-3-one–MeOH complex (1:1) and 2β,17β-diacetoxy-4-androsten-3-one–*p*-bromophenol complex (1:1), the A-rings of the steroids have been determined to be in an inverted half-chair conformation. This conformation is in sharp contrast to the normal half-chair conformation observed in the crystal structures of 14 other $\Delta^4$-3-one steroids including one with a 2β-Cl substituent. Steric interaction between the 19-Me substituent and the acetate group in the 2β position may be the cause of this surprising conformational difference. In the inverted half-chair arrangement, the conjugation of the α,β-unsaturated ketone system in the A-ring is disrupted, atoms O(2), C(2), C(3), and O(3) achieve a nearly coplanar arrangement, and atoms C(3), C(4), C(5), C(10), and C(1) also reside in nearly coplanar positions. This combination of the two coplanar arrangements of atoms may be an energetically favorable conformation and suggests that the inverted half-chair may also constitute a stable form of these molecules in solution.

From the interpretation of ORD, CD, and nmr measurements, the A-rings of some derivatives of testosterone having 2β substituents were predicted to be in a half-boat or "nonsteroidal" half-chair or twist conformation.[1b-3] Because steroid A-rings containing the 4-en-3-one system were found to be in the normal half-chair conformation in 14 molecular structures determined by X-ray crystallography† and because the boat form is energetically less favorable, we have undertaken the structural investigation of some of the steroids in which the A-ring is predicted to be in the half-boat conformation. The first such structure investigated, 2,2,6β-trichlorotestosterone acetate,[8,‡] was found to have the conventional half-chair conformation of the A-ring in conflict with the previous interpretation of ORD, CD, and nmr spectra.[3,17]

The conformation of the A-ring in 2β-hydroxytestosterone is of particular interest as this steroid is a natural metabolite of testosterone and a possible intermediate in the biosynthesis of 2-oxygenated estrogens. Since crystals of 2β-hydroxytestosterone suitable for X-ray analysis could not be obtained, and since the ORD and CD spectra of the acetate[1b] and chloroacetate[18] of 2β-hydroxytestosterone indicated that the B-ring conformation of this steroid would be the same as that of the free compound, the crystal structures of 2β-hydroxytestosterone 2-acetate 17-chloroacetate (I) (Figure 1)–methanol complex and 2β-hydroxytestosterone diacetate (II)–*p*-bromophenol complex were determined in order to obtain definitive information concerning the A-ring conformation in this group of steroids.

**A-Ring Conformation.**—In both crystalline modifications the A-ring of 2β-hydroxytestosterone diester is in a conformation which is best described as an inverted half-chair or a 6-membered envelope with atom C(2) being the tip on the α side of the general plane of ring A. Projections of A-rings in various conformations viewed parallel to the C(5)–C(10) bond are presented in Figure 2. The inverted half-chair conformation of the ring observed in the esters (a) is contrasted with the more commonly occurring half-chair conformations found in the structures of testosterone–*p*-bromophenol complex (b),[10] 2,2,6β-trichlorotestosterone acetate (c), and 9α-bromo-17β-hydroxy-17α-methyl-4-androstene-3,11-dione (d),[16] and a hypothetical half-boat conformation of a cyclohexenone A-ring (e).

Atoms C(1), C(3), C(4), C(5), and C(10) in I and II are within 0.09 Å of a least-squares plane. The deviations of individual atoms in the A-ring from this plane (Table I) are compared with the average deviations from planarity of these atoms in the $\Delta^4$-3-one containing

† 17β-Trimethylsiloxy-4-androsten-3-one,[4] 17β-bromoacetoxy-7α-methyl-4-estren-3-one,[5] 4-chloro-17,21-dihydroxy-4-pregnene-3,11,20-trione,[6] 17β-bromoacetoxy-9β,10α-androst-4-en-3-one,[7] 2,2,6β-trichloro-17β-acetoxy-4-androsten-3-one,[8] 17aβ-*p*-bromobenzenesulfonyloxy-17α-methyl-D-homo-9β,10α-estr-4-en-3-one,[9] 17β-hydroxy-4-androsten-3-one–*p*-bromophenol complex (1:1),[10] 17β-(*p*-bromobenzoyloxy)-4-androsten-3-one,[11] 17β-bromoacetoxy-8β-methyl-4-androsten-3-one,[11] 6β-bromo-4-pregnene-3,20-dione,[12] 17β-hydroxy-4-androsten-3-one–mercuric chloride complex (2:1),[13] 12α-bromo-11β-hydroxy-4-pregnene-3,20-dione,[14] 22,23-dibromo-9β-ergost-4-en-3-one,[15] 9α-bromo-17β-hydroxy-17α-methyl-4-androstene-3,11-dione.[16]

‡ Abbreviations used are: 2β-hydroxytestosterone 2-acetate 17-chloroacetate, 2β-acetoxy-17β-chloroacetoxy-4-androsten-3-one; 2β-hydroxytestosterone diacetate, 2β,17β-diacetoxy-4-androsten-3-one; 2,2,6-trichlorotestosterone acetate, 2,2,6β-trichloro-17-acetoxy-4-androsten-3-one; 2β-hydroxy-19-nortestosterone, 2β,17β-dihydroxy-4-estren-3-one; testosterone, 17β-hydroxy-4-androsten-3-one.

(1) (a) Faculty Research Awardee, PRA-72, of the American Cancer Society; (b) S. L. Patashnik, H. L. Kimball, and S. Burstein, *Steroids*, **2**, 19 (1963); K. Kuriyama, E. Kondo, and K. Tori, *Tetrahedron*, **22**, 1485 (1963).

(2) Y. Yamato and H. Kaneko, *ibid*, **21**, 2501 (1965).

(3) Y. Kondo, K. Kondo, T. Tahemoto, K. Yasuda, and G. Snatzke, *ibid.*, **21**, 1191 (1965).

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(6) W. L. Duax, A. Cooper, and D. A. Norton, *Acta Crystallogr., Sect. B*, **26**, in press (1970).

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(10) A. Cooper, G. Kartha, E. M. Gopalakrishna, and D. A. Norton, *Acta Crystallogr., Sect. B*, **25**, 2409 (1969).

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(14) A. Cooper and D. A. Norton, *ibid., Sect. B*, **24**, 811 (1968).

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(16) A. Cooper, C. T. Lu, and D. A. Norton, *J. Chem. Soc. B*, 1228 (1968).

(17) Y. Kondo, T. Takemoto, and K. Yasuda, *Chem. Pharm. Bull. (Tokyo)*, **12**, 976 (1964).

(18) Compound I, mp 190–191°, $\lambda_{max}^{ethanol}$ 244 mμ (ε 15,300), was prepared from testosterone chloroacetate by bromination followed by acetolysis. The details of the synthesis and the hydrolysis products are to be published by Y. Osawa and J. O. Gardner.

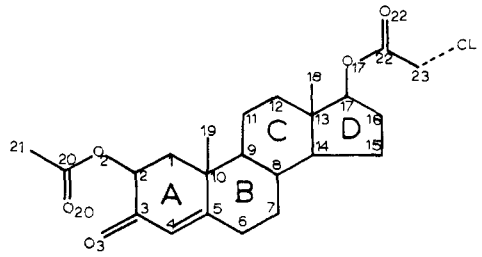


Figure 1.—Atomic numbering and ring nomenclature for 2β-hydroxytestosterone 2-acetate 17-chloroacetate.

TABLE I

DEVIATIONS OF INDIVIDUAL ATOMS FROM LEAST-SQUARES PLANES THROUGH ATOMS C(1), C(3), C(4), C(5), AND C(10) OF STEROIDS HAVING CYCLOHEXENONE A-RINGS

| Atoms included in least-squares plane | Atoms for which distance calculated | Distances from plane,[a] Å I | II | III |
|---|---|---|---|---|
| C(1), C(3), C(4), C(5), C(10) | C(1) | 0.078 | 0.093 | −0.14 |
| | C(3) | −0.066 | −0.081 | 0.12 |
| | C(4) | 0.043 | 0.062 | −0.09 |
| | C(5) | 0.036 | 0.033 | −0.05 |
| | C(10) | −0.093 | −0.107 | 0.16 |
| | C(2) | −0.615 | −0.562 | 0.48 |
| | C(6) | −0.030 | 0.007 | −0.15 |
| | O(3) | 0.243 | 0.228 | 0.11 |

[a] The tabulated distances are (I) 2β-hydroxytestosterone 2-acetate 17-chloroacetate, (II) 2β-hydroxytestosterone diacetate, and (III) average values for 14 steroids in which the A-rings show only minor deviations from the normal half-chair conformation.

steroids having the normal half-chair conformation of the A-ring.

Of the atoms in the A-ring, C(2) is seen to have the largest deviation from this plane, residing on the β side of the plane in the steroids having the normal half-chair A-ring conformation and on the α side of the plane when the A-ring is in the inverted half-chair conformation. Atoms O(2), C(2), C(3), and O(3) are planar to within 0.09 Å in both esters and the O(2)–O(3) interatomic distance of 2.72 Å is of H-bonding order. An intramolecular H bond between O(2) and O(3) has been considered as a possible stabilizing feature of "twist" and half-boat conformations of the A-ring of 2β-hydroxy-Δ⁴-3-keto steroids.[1,19] However, even when atoms O(2), C(2), C(3), and O(3) are in a planar conformation, as is the case in the inverted half-chair conformation, the required C(2)–O(2)–H(O2) bond angle of approximately 109° would prevent any effective overlap of the van der Waals radii of atoms H(O2) and O(3). The O(2)–H(O2)...O(3) angle of approximately 90° would be far short of the 135° minimum generally accepted as necessary for H bonding.[20]

The inverted half-chair conformation disrupts the Δ⁴-3-one conjugated system. When the A-ring is in the normal half-chair conformation the α,β-unsaturated ketone system can achieve complete conjugation, as was observed in the structure of 2,2,6β-trichlorotestosterone acetate in which the seven atoms [C(2), C(3), C(4), C(5), C(6), C(10), and O(3)] involved in the

(19) H. J. Brodie and A. Pillai, "Program of 51st Meeting of the Endocrine Society," 1969, p 79.

(20) J. Donohue in "Structural Chemistry and Molecular Biology," A. Rich and N. Davidson, Ed., W. H. Freeman, San Francisco, Calif., 1968, pp 232–234.

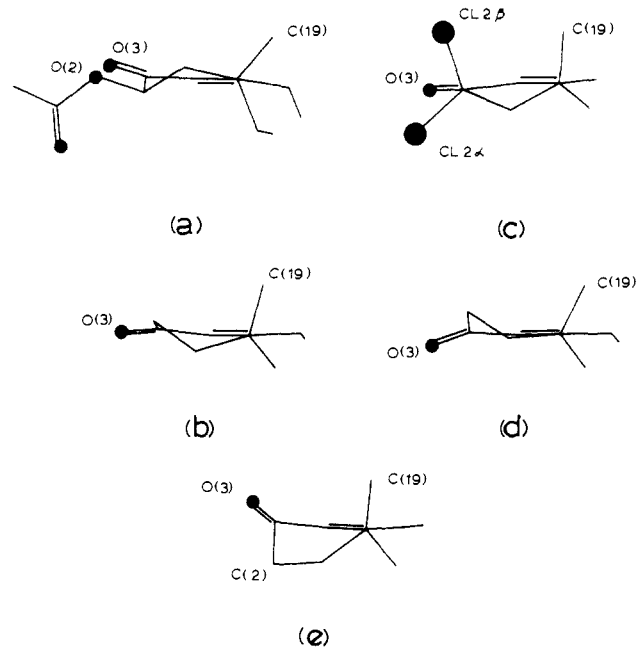


Figure 2.—Steroid A-rings containing the 4-en-3-one system projected parallel to the C(5)–C(10) bond in 2β-hydroxytestosterone 2-acetate 17-chloroacetate (a), testosterone-*p*-bromophenol (b), 2,2,6β-trichlorotestosterone acetate (c), 9α-bromo-17α-methyl-11-oxotestosterone (d), and a hypothetical half-boat conformation (e).

conjugated system were planar to within ±0.04 Å. The atoms immediately involved in the double bond conjugation, O(3), C(3), C(4), and C(5), are almost always planar to within 0.03 Å. Of the structures with the half-chair A-ring conformation, only two exhibit any pronounced breakdown of the conjugation of the double bond demonstrated by a loss of planarity of these 4 atoms. In 22,23-dibromo-9β-ergost-4-en-3-one[15] the strain associated with the twist-boat conformations of the B- and C-rings is transmitted to the A-ring, and in 9α-bromo-17β-hydroxy-17α-methyl-4-androstene-3,11-dione[16] the flattening of the B- and C-rings caused by the 9α-halogen results in the pronounced arching of the A-ring toward the α side of the steroid. The deviations of individual atoms from a least-squares plane through atoms O(3), C(3), C(4), and C(5) in structures I and II as well as other crystallographically determined structures are given in Table II. The 12 structures in which these atoms are essentially planar are combined in column III. Columns IV and V are the A-ring half-chair structures which do not exhibit total conjugation of the α,β-unsaturated ketone system.

The O(3)–C(3)–C(2)–R(2β) torsion angles for 4-chlorocortisone, 2,2,6β-trichlorotestosterone, and 2β-hydroxytestosterone 2,17-diacetate are illustrated in Figure 3. Compounds I and II have torsion angles of 16.2° and 16.0° indicating that the 2β substituent is in an equitorial position. If the 2β-hydrogen position in 4-chlorocortisone is representative of the normal position of a 2β substituent on the 4-en-3-one steroid in the half-chair conformation, the 74° torsion angle in 2,2,6β-trichlorotestosterone acetate molecule indicates some strain in the A-ring of that structure. The strain introduced between the 2β-AcO and 19-Me groups, coupled with the energetic favorability of a planar conformation of atoms O(2), C(2), C(3), and

TABLE II

DEVIATIONS OF INDIVIDUAL ATOMS FROM LEAST-SQUARES PLANES THROUGH ATOMS C(3), C(4), C(5), AND O(3) OF STEROIDS HAVING CYCLOHEXENONE A-RINGS

| Atoms included in least-squares plane | Atoms for which distance calculated | Distances from plane,[a] Å | | | | |
|---|---|---|---|---|---|---|
| | | I | II | III | IV | V |
| C(3), C(4), C(5), O(3) | C(3) | −0.09 | −0.07 | −0.03 to +0.04 | −0.08 | 0.09 |
| | C(4) | −0.08 | −0.07 | −0.03 to +0.04 | −0.07 | 0.08 |
| | C(5) | 0.08 | 0.07 | −0.04 to +0.03 | 0.07 | −0.08 |
| | O(3) | 0.09 | 0.08 | −0.04 to +0.03 | 0.08 | −0.09 |
| | C(2) | −0.35 | −0.19 | −0.04 to +0.36 | −0.23 | 0.39 |
| | C(6) | −0.11 | −0.12 | −0.07 to +0.33 | 0.19 | 0.01 |
| | C(10) | 0.25 | 0.31 | −0.21 to +0.16 | 0.15 | −0.36 |

[a] The tabulated distances are (I) 2β-hydroxytestosterone 2-acetate 17-chloroacetate, (II) 2β-hydroxytestosterone diacetate, (III) average values for 12 steroids in which the A-rings show only minor deviations from the half-chair conformation, (IV) 22,23-dibromo-9β-ergost-4-en-3-one, and (V) 9α-bromo-17β-hydroxy-17α-methyl-4-androstene-3,11-dione.

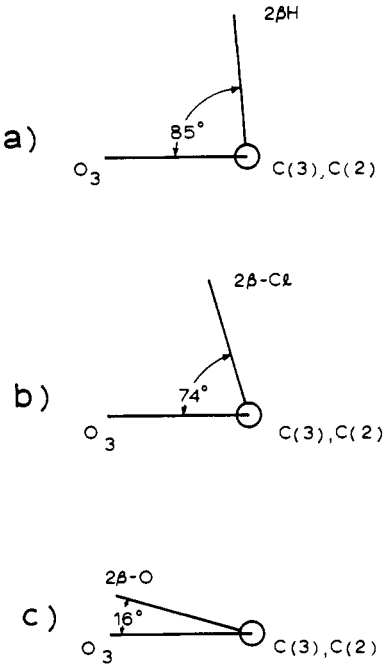


Figure 3.—The O(3)-C(3)-C(2)-R(2β) torsional angles in 4-chlorocortisone (a), 2,2,6β-trichlorotestosterone acetate (b), and 2β-hydroxytestosterone diacetate (c).

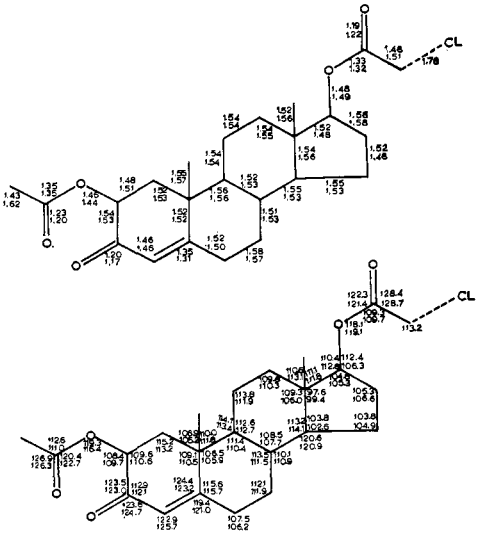


Figure 4.—Interatomic distances and angles in the two molecules. In each case the top value is for 2β-hydroxytestosterone 2-acetate 17-chloroacetate and the standard deviations are approximately 0.01 Å for distances and 0.8° for angles. The bottom value is for 2β-hydroxytestosterone diacetate and the standard deviations are 0.02 Å for distances and 1.2° for angles.

O(3) may provide enough energy to disrupt the conjugated double bond system and successfully adopt the inverted half-chair conformation. Elucidation of the structure of the 2β-OH derivatives of testosterone and 19-nortestosterone should provide additional information concerning the stability of the inverted half-chair A-ring conformation.

**Steroid Conformation.**—All important intramolecular bonds and angles for the two structure determinations are compared in Figure 4. The average standard deviations in bonds and angles are ±0.01 Å and ±0.8° for I and ±0.02 Å and ±1.2° for II. None of the values for bonds and angles in the steroid nucleus are significantly different from those observed in similar molecules. All bonds and angles of the *p*-bromophenol complex, except for the terminal C–C bond in the acetate group bonded to C(2), are within 3 standard deviations of the corresponding values in the more accurate 2β-hydroxytestosterone 2-acetate 17-chloroacetate structure. The increase in the C(20)–C(21) bond length may be correlated with a close contact of the Br of an adjacent *p*-bromophenol molecule to the C=O. This 3.27 Å Br–O distance is 0.08 Å less than the sum of the van der Waals radii. Approximately 15% of the *p*-bromophenol molecules in the crystal lattice are disordered (see Molecular Packing). The nature of the disorder is a minor translational shift which results in an increase in this Br–O contact length to 3.43 Å.

The B- and C-rings are in conventional chair conformations and the D-ring has a conformation intermediate between a β-envelope and a half-chair. This conformation can be described by the parameters $\Delta$ = 23.6 and $\phi_m$ = 48.2.[21] In Table III, torsion angles of the rings are compared for the two crystalline derivatives of 2β-hydroxytestosterone and contrasted with those of testosterone found in the structure of testosterone–*p*-bromophenol (1:1) complex.[10] From inspection of the torsion angles, it is apparent that the crystal environment in these structures has almost no effect upon the conformation of the steroid nucleus and that the conformational change in the A-ring has little effect on the steroid beyond the A/B ring junction. The reversal of signs on the torsion angles of the A-ring is another characteristic of the half-chair inversion.

(21) C. Altona, J. J. Geise, and C. Romers, *Tetrahedron*, **24**, 13 (1968).

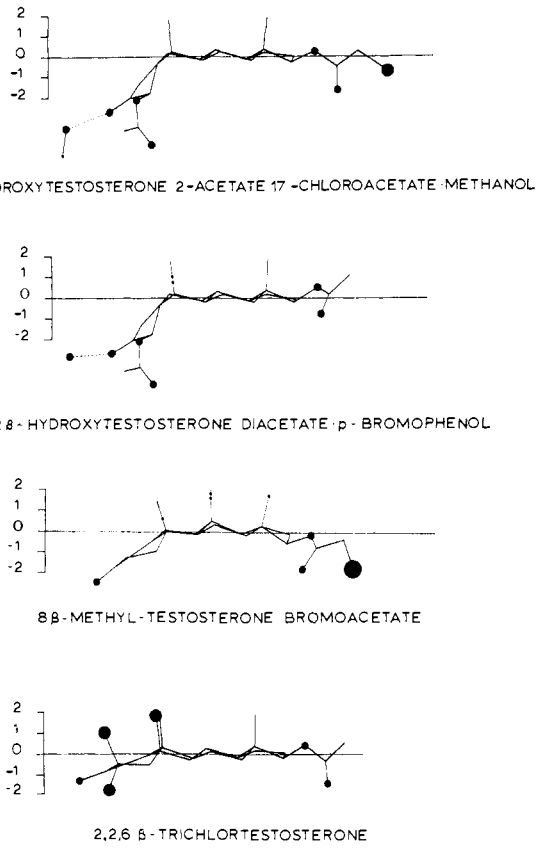


Figure 5.—Projection parallel to the least-squares plane through atoms C(5)–C(17) of 2β-hydroxytestosterone 2-acetate 17-chloroacetate (a), 2β-hydroxytestosterone diacetate (b), 8β-methyltestosterone bromoacetate (c), and 2,2,6β-trichlorotestosterone (d).

While the steroid nuclei of the two crystalline modifications under investigation were unaltered by variation of environment, the orientation of the side chain bonded to C(17) was quite perceptibly altered. This is illustrated in Figure 5 which is a projection of the molecules parallel to the least-squares planes through atoms C(5) to C(17). The orientations of the acetate side chains in the structures of 8β-methyltestosterone bromoacetate[11] and 2,2,6β-trichlorotestosterone acetate are also shown in Figure 5 in order to illustrate that the variation of the acetate orientation is not necessarily correlated with the heavy-atom substitution on the side chain. The variation in the magnitude of the dihedral angles (Table IVa) between the least-squares planes through the atoms of the 17 side chain and the atoms of the planar portion of the D-ring for these four molecules is a quantitative expression of the flexibility of the orientation of the 17-acetate side chain. The equivalence of the dihedral angles between the acetate group at C(2) and the planar configuration of O(2), C(2), C(3), and O(3) (Table IVb) indicates that the effect of the crystal environment upon the orientation of this side chain is minimal. This excellent conformational agreement is especially interesting in view of the disorder of the *p*-bromophenol in this region of complex II.

**Molecular Packing and Hydrogen Bonding.**—The dramatic contrast in the packing arrangement of the molecules in the two derivatives is illustrated in Figure 6. In the structure of 2β-hydroxytestosterone diacetate, the *p*-bromophenol molecules and the B-, C-, and D-rings of the steroid lie in planes which are parallel to one another. The 2.73 Å H bonds linking phenols to steroid molecules, the 3.27 Å Br–O contacts, and other intermolecular contacts less than 3.7 Å are indicated in Figure 6a, which is a projection down the *a* crystallographic axis. The disordered *p*-bromophenol molecules (not shown in Figure 6) are nearly superimposable upon the ordered *p*-bromophenol in this projection and are translated 0.5 Å parallel to the *a* axis, increasing the H bond length to 3.00 Å and the Br–O contact distance to 3.43 Å in 15% of the crystal lattice. The 2β-hydroxytestosterone 2-acetate 17-chloroacetate structure has been projected parallel to the C(7)–C(11) vector in Figure 6b. Although the H bond is slightly shorter (2.69 Å) and similarly oriented with regard to

TABLE III

TORSIONAL ANGLES IN THE RINGS[a]

| Ring A | I, deg | II, deg | III, deg |
|---|---|---|---|
| C(1)–C(2) | 60.0 | 58.3 | −56.1 |
| C(2)–C(3) | −45.7 | −42.4 | 34.8 |
| C(3)–C(4) | 18.1 | 12.1 | −4.0 |
| C(4)–C(5) | −1.1 | 4.7 | −5.8 |
| C(5)–C(10) | 11.8 | 9.7 | −16.5 |
| C(10)–C(1) | −41.9 | −40.9 | 46.1 |
| Ring B | | | |
| C(5)–C(6) | −58.4 | −61.0 | −52.3 |
| C(6)–C(7) | 51.9 | 55.0 | 53.6 |
| C(7)–C(8) | −53.3 | −56.0 | −62.9 |
| C(8)–C(9) | 55.2 | 56.8 | 67.1 |
| C(9)–C(10) | −55.2 | −56.8 | −60.1 |
| C(10)–C(5) | 60.0 | 62.4 | 54.0 |
| Ring C | | | |
| C(8)–C(9) | −52.3 | −53.4 | −52.0 |
| C(9)–C(11) | 53.2 | 54.5 | 49.3 |
| C(11)–C(12) | −54.0 | −57.1 | −55.4 |
| C(12)–C(13) | 55.8 | 58.4 | 59.6 |
| C(13)–C(14) | −59.9 | −62.1 | −60.8 |
| C(14)–C(8) | 57.2 | 59.3 | 56.4 |
| Ring D | | | |
| C(13)–C(14) | 48.3 | 45.7 | 45.4 |
| C(14)–C(15) | −33.8 | −34.8 | −33.4 |
| C(15)–C(16) | 5.1 | 10.5 | 7.7 |
| C(16)–C(17) | 25.5 | 19.1 | 21.7 |
| C(17)–C(13) | −44.9 | −39.2 | −40.8 |

[a] The tabulated torsion angles are those in (I) 2β-hydroxytestosterone 2-acetate 17-chloroacetate, (II) 2β-hydroxytestosterone diacetate, and (III) testosterone as found in a testosterone *p*-bromophenol complex.[10]

TABLE IV

DIHEDRAL ANGLES INVOLVING ACETATE SIDE CHAINS

| Structure | Dihedral angle, deg |
|---|---|
| a. Dihedral Angles between the Least-Squares Planes through Atoms O(17), C(22), O(22), and C(23) and the Least-Squares Planes through Atoms C(14), C(15), C(16), and C(17) | |
| 8β-Methyltestosterone bromoacetate | 44 |
| 2β-Hydroxytestosterone diacetate | 52 |
| 2,2,6β-Trichlorotestosterone acetate | 90 |
| 2β-Hydroxytestosterone 2-acetate 17-chloroacetate | 96 |
| b. Dihedral Angles between the Least-Squares Planes through Atoms O(2), C(20), O(20), and C(21) and the Least-Squares Planes through Atoms O(2), C(2), C(3), and O(3) | |
| 2β-Hydroxytestosterone diacetate | 21.6 |
| 2β-Hydroxytestosterone 2-acetate 17-chloroacetate | 20.9 |

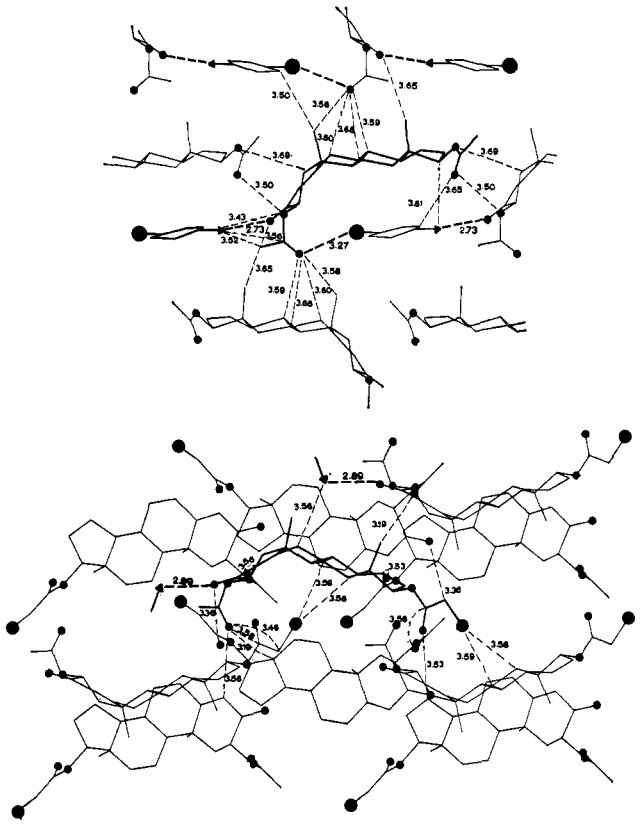

Figure 6.—Immediate crystalline environment of 2β-hydroxytestosterone diacetate (a) and 2β-hydroxytestosterone 2-acetate 17-chloroacetate (b).

the steroid molecule in both crystal lattices, the rest of the molecular environment is vastly different as is indicated by the nature of the closest contacts. In the *p*-bromophenol complex all contacts less than 3.7 Å are with the β face of the steroid, while in the methanol complex most close contacts are to the sides of the molecule.

## Experimental Section

Pertinent crystal data are presented in Table V. Crystals of both complexes were enclosed in capillaries to prevent decomposition during data collection. The unit cell constants were determined from least-squares refinements of three-dimensional vector (eight per parameter) having $2\theta > 60°$. The density was measured by flotation of the crystals in an aqueous potassium iodide solution. Intensities were measured by the stationary-crystal–stationary-counter method[22] (Cu K$\alpha$ = 1.5418 Å). Since the background intensity was a uniform function of $2\theta$ above 40°, balanced nickel and cobalt filter measurements of 10% of the data were used to construct a background correction curve. Lorentz and polarization corrections were applied.

The elongated *b* axes of the crystals were mounted parallel to the $\phi$ axis of the diffractometer. The shape anisotropy measurements at $\chi = 90°$ were found to be less than ±3% in I and ±8% in II over the $\phi$ range covered in intensity collection. No absorption correction was deemed necessary because the primary motivation for this investigation was to determine molecular conformation and geometry of the steroid which was well established in the more accurate determination (I) and corroborated in the other (II).

The structures were solved by straightforward application of the heavy-atom method.[23] Atomic scattering factors were taken from International Tables for X-Ray Crystallography.[24] The positional parameters and anisotropic thermal parameters of all nonhydrogen atoms were refined by least squares, using a block diagonal approximation to the least-squares normal equations. Structure I refined readily to an *R* (defined as $\Sigma||F_o| - |F_c||/\Sigma|F_o|$) of 9.8%. Structure II refined to an *R* of 11% before a three-dimensional, electron-density difference map revealed the presence of the disordered *p*-bromophenol molecules. Introducing atoms having 15% occupancy at the secondary *p*-bromophenol

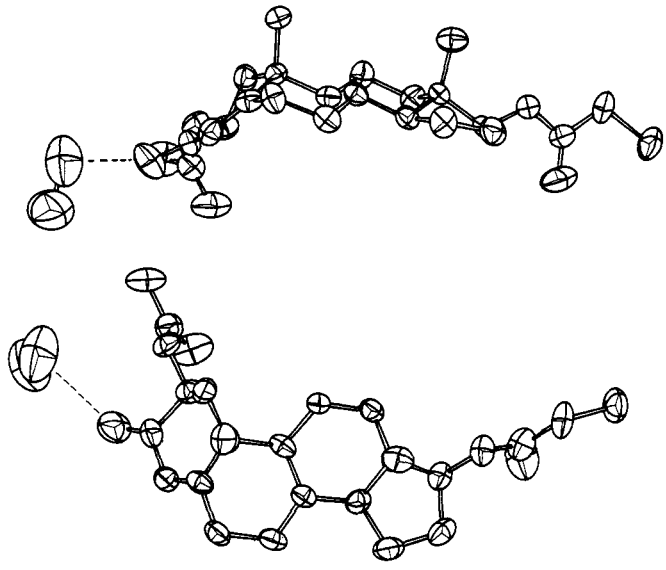

Figure 7.—Perspective views of a molecule of 2β-hydroxytestosterone 2-acetate 17-chloroacetate-methanol, showing 50% probability thermal vibration ellipsoids.

TABLE V

CRYSTAL DATA FOR (I) 2β-HYDROXYTESTOSTERONE 2-ACETATE 17-CHLOROACETATE–METHANOL AND (II) 2β-HYDROXYTESTOSTERONE DIACETATE–*p*-BROMOPHENOL

| | I | II |
|---|---|---|
| Molecular formula | $C_{23}H_{31}ClO_5 \cdot CH_3OH$ | $C_{23}H_{32}O_5 \cdot BrC_6H_4OH$ |
| Molecular weight | 422.9·32.0 | 388.5·173.0 |
| Crystal system | Orthorhombic | Monoclinic |
| Space group | $P2_12_12_1$ | $P2_1$ |
| *Z* | 4 | 2 |
| Cell dimensions, Å | $a = 13.458 \pm 0.002$ | $a = 10.862 \pm 0.003$ |
| | $b = 16.632 \pm 0.003$ | $b = 16.844 \pm 0.004$ |
| | $c = 10.768 \pm 0.002$ | $c = 7.574 \pm 0.002$ |
| | | $\beta = 92.10 \pm 0.005°$ |
| Cell volume, Å$^3$ | 2410.1 | 1384.88 |
| Measured density, g/cm$^3$ | 1.27 | |
| Calculated density, g/cm$^3$ | 1.25 | 1.34 |
| Linear absorption coefficient cm$^{-1}$ | 17.0 | 25.6 |
| *F*(000) | 976 | 588 |
| Crystal size, mm | 0.20 × 0.25 × 0.20 | 0.25 × 0.33 × 0.20 |
| Solvent | Methanol | Hexane |
| Final *R* | | |
| Total reflections measured, % | 9.8 (2398) | 10.4 (2781) |
| Reflections above background, % | 8.0 (1870) | 8.3 (2030) |

(22) T. C. Furnas, "Single Crystal Orienter Manual," General Electric Co., Milwaukee, Wis., 1957.

(23) H. Lipson and W. Cochran, "The Determination of Crystal Structures, The Crystalline State," Vol. III, Bell, London, 1953.

(24) International Tables for X-Ray Crystallography, Vol. I, The Kynoch Press, Birmingham, England, 1962.

TABLE VI

POSITIONAL PARAMETERS OF THE NONHYDROGEN ATOMS IN THE METHANOL COMPLEX (I) AND THE *p*-BROMOPHENOL COMPLEX (II). THE STANDARD DEVIATION IN THE LAST TWO DIGITS ARE GIVEN IN PARENTHESES

| | I | | | II | | |
|---|---|---|---|---|---|---|
| | X/A | Y/B | Z/C | X/A | Y/B | Z/C |
| C 1 | 0.6798 ( 6) | 0.8262 ( 4) | 0.6642 ( 7) | -0.0998 ( 9) | 0.5695 ( 6) | 0.6643 (12) |
| C 2 | 0.7285 ( 5) | 0.7821 ( 4) | 0.7672 ( 7) | -0.1202 ( 9) | 0.6562 ( 7) | 0.6188 (14) |
| C 3 | 0.6488 ( 6) | 0.7449 ( 4) | 0.8520 ( 7) | -0.1774 (10) | 0.6650 ( 8) | 0.4318 (15) |
| C 4 | 0.5688 ( 5) | 0.8009 ( 4) | 0.8820 ( 7) | -0.1208 (10) | 0.6115 ( 8) | 0.3059 (14) |
| C 5 | 0.5510 ( 5) | 0.8683 ( 5) | 0.8155 ( 7) | -0.0470 ( 9) | 0.5524 ( 7) | 0.3465 (13) |
| C 6 | 0.4740 ( 5) | 0.9284 ( 5) | 0.8621 ( 8) | 0.0193 ( 9) | 0.5082 ( 8) | 0.2060 (12) |
| C 7 | 0.5299 ( 5) | 1.0072 ( 5) | 0.8964 ( 7) | 0.1601 ( 9) | 0.5240 ( 7) | 0.2431 (12) |
| C 8 | 0.5956 ( 5) | 1.0364 ( 4) | 0.7916 ( 7) | 0.2011 ( 9) | 0.5012 ( 6) | 0.4322 (12) |
| C 9 | 0.6676 ( 4) | 0.9728 ( 4) | 0.7441 ( 6) | 0.1249 ( 8) | 0.5445 ( 6) | 0.5691 (11) |
| C10 | 0.6119 ( 5) | 0.8949 ( 4) | 0.7040 ( 7) | -0.0164 ( 8) | 0.5267 ( 6) | 0.5358 (12) |
| C11 | 0.7394 ( 6) | 1.0057 ( 5) | 0.6456 ( 7) | 0.1710 (10) | 0.5280 ( 8) | 0.7606 (11) |
| C12 | 0.7962 ( 5) | 1.0816 ( 4) | 0.6872 ( 7) | 0.3092 ( 8) | 0.5472 ( 7) | 0.7888 (11) |
| C13 | 0.7222 ( 5) | 1.1459 ( 4) | 0.7309 ( 6) | 0.3863 ( 8) | 0.4989 ( 6) | 0.6576 (11) |
| C14 | 0.6563 ( 5) | 1.1109 ( 4) | 0.8341 ( 7) | 0.3363 ( 8) | 0.5224 ( 6) | 0.4691 (10) |
| C15 | 0.6033 ( 6) | 1.1856 ( 5) | 0.8894 ( 8) | 0.4366 ( 9) | 0.4912 ( 8) | 0.3507 (12) |
| C16 | 0.6802 ( 7) | 1.2519 ( 4) | 0.8782 ( 8) | 0.5520 ( 9) | 0.5023 ( 8) | 0.4541 (12) |
| C17 | 0.7686 ( 6) | 1.2136 ( 4) | 0.8063 ( 7) | 0.5156 ( 9) | 0.5249 ( 7) | 0.6446 (12) |
| C18 | 0.6634 ( 6) | 1.1789 ( 5) | 0.6219 ( 7) | 0.3765 (11) | 0.4071 ( 7) | 0.6849 (16) |
| C19 | 0.5423 ( 6) | 0.9131 ( 5) | 0.5928 ( 8) | -0.0462 (10) | 0.4364 ( 7) | 0.5575 (16) |
| C20 | 0.8684 ( 6) | 0.6905 ( 5) | 0.7758 ( 8) | -0.1934 (11) | 0.7639 ( 7) | 0.7861 (14) |
| C21 | 0.9204 ( 8) | 0.6287 ( 7) | 0.7099 (10) | -0.2891 (16) | 0.7883 (10) | 0.9182 (19) |
| C22 | 0.8946 ( 6) | 1.3136 ( 5) | 0.7694 ( 8) | 0.6261 ( 9) | 0.5097 ( 7) | 0.9263 (13) |
| C23 | 0.9291 ( 8) | 1.3717 ( 5) | 0.6750 (10) | 0.7024 (13) | 0.4507 (11) | 1.0340 (18) |
| C24 | 0.7535 (17) | 0.4881 (15) | 0.9413 (19) | -0.2038 ( 7) | 0.6862 ( 5) | 0.7454 (10) |
| O 2 | 0.7877 ( 4) | 0.7170 ( 3) | 0.7141 ( 5) | -0.2621 ( 8) | 0.7064 ( 5) | 0.3984 (13) |
| O 3 | 0.6514 ( 5) | 0.6770 ( 4) | 0.8881 ( 6) | 0.6018 ( 6) | 0.4808 ( 5) | 0.7671 ( 9) |
| O17 | 0.8187 ( 4) | 1.2717 ( 3) | 0.7237 ( 5) | -0.1167 (10) | 0.8063 ( 6) | 0.7248 (14) |
| O20 | 0.8929 ( 5) | 0.7215 ( 5) | 0.8752 ( 6) | 0.5834 ( 9) | 0.5732 ( 6) | 0.9729 ( 9) |
| O22 | 0.9255 ( 6) | 1.3032 ( 5) | 0.8718 ( 7) | 0.7635 (13) | 0.2441 (10) | 0.8358 (19) |
| O24 | 0.7174 (13) | 0.5171 ( 7) | 0.8301 (15) | 0.6416 (15) | 0.2237 ( 9) | 0.8811 (22) |
| CL | 1.0384 ( 1) | 1.4241 ( 1) | 0.7198 ( 2) | 0.5520 (13) | 0.2214 ( 8) | 0.7506 (19) |
| | | | | 0.5767 (13) | 0.2410 ( 9) | 0.5746 (18) |
| | | | | 0.6909 (13) | 0.2599 (11) | 0.5349 (20) |
| | | | | 0.7910 (14) | 0.2628 (11) | 0.6547 (26) |
| | | | | 0.4813 (10) | 0.2381 ( 8) | 0.4511 (13) |
| | | | | 0.1121 ( 2) | 0.7500 ( 2) | 0.9840 ( 3) |

position allowed the refinement to proceed to an $R$ of 9.4%. In electron-density difference maps 33 of the 37 H atoms of the *p*-bromophenol complex and all H in structure I except those on the C atom of the methanol molecule were located. Holding H atom positional and thermal parameters constant two cycles of refinement on all data, using a weighting scheme of the form $1/\{1 + [(|F_o| - 15)/15]^2\}$ which made the average weighted squares of $(|F_o| - |F_c|)$ at different ranges of $|F_o|$ nearly equal, resulted in final $R$ factors of 8.0 and 8.3% for observed data in I and II, respectively.

Positional parameters for all non-H atoms are listed in Table VI. Anisotropic thermal parameters for non-H atoms and H atom positional parameters and lists of observed and calculated structure factors are available from the authors upon request.

Figure 7 presents two perspective views of molecule I in which ellipsoids describe the anisotropic thermal motion of the atoms as observed in the crystal structure. Comparison of these diagrams with those of 12-$\alpha$-bromo-11$\beta$-hydroxyprogesterone for which a thorough analysis of the thermal motion has been reported[14] suggests that the molecular motion is roughly consistent with molecular librations about the principal axes of inertia of the steroid.

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