This holds as long as $m \ll a$.

Appendix II

Consider the equilibrium in eq A6, where HA is enol acetylacetone. If m equals the total Mn(II) present and a is equal to the total acetylacetone enol form species present, then $a = [HA] + [MnA^+] + [MnA_2]$ ($[A^-]$ is extremely small at the pH's used in this study) and $m = [Mn^{2+}] + [MnA^+] + [MnA_2]$. $[MnA_2]$ under the conditions of the experiments is small in comparison to $[Mn^{2+}]$ and $[MnA^+]$ and is neglected here. Then, if activity coefficients are assumed to be unity,

$$Mn^{2+} + HA \rightleftharpoons MnA^+ + H^+$$

$$K_{ass_1} = \frac{(MnA^+)(H^+)}{(Mn^{2+})(HA)} \qquad (A6)$$

$$K_{ass_1} = \frac{[MnA^+][H^+]}{(m - [MnA^+])(a - [MnA^+])}$$

and

$$am - (a + m + (H^+)/K_{ass_1})[MnA^+] + [MnA^+]^2 = 0$$

From Appendix I we see that $a \gg [MnA^+]$ and $\gg m$, at the highest m concentration used, and is at least 10 times the concentration of MnA^+. Therefore $[MnA^+]^2 \ll a[MnA^+]$ and

$$\frac{m}{a + m + (H^+)/K_{ass_1}} \simeq \frac{[MnA^+]}{a} \simeq P_{B_1}$$

where P_{B_1} is the mole fraction of the enol form of acetylacetone that is bound.

A similar treatment for association of the Mn(II) with the diketo form of acetylacetone, without proton loss, can be developed. Following the same lines, one can derive the parallel expression of eq A7, where P_{B_2} is the mole fraction of the diketo form of acetylacetone that is bound, k is the concentration of the diketone form, and K_{ass_2} is the association constant between Mn(II) and the diketone form. In this and in the previous corresponding expression for the mole fraction of the enol form it appears that the concentrations k and a in the denominator are negligible with respect to $1/K_{ass_2}$ and $(H^+)/K_{ass_1}$, respectively, since the slopes (Table II) are relatively independent of a substantial change in k or a.

$$P_{B_2} = \frac{[MnK^{2+}]}{k} \simeq \frac{m}{k + m + 1/K_{ass_2}} \qquad (A7)$$

Registry No. Acetylacetone, 123-54-6; acetylacetone enol, 1522-20-9; (*Z*)-maleylacetone, 40609-69-6; (*Z,E*)-maleylacetone enol, 77415-36-2; (*Z,Z*)-maleylacetone enol, 25568-65-4; 3,3-dimethyl-2,4-pentanedione, 3142-58-3; acetone, 67-64-1.

Conformational Analysis of Steroids: Polymorphic Forms of 17β-Acetoxy-6β-bromo-4-androsten-3-one

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X-ray crystal structure analysis of two polymorphic forms of 17β-acetoxy-6β-bromo-4-androsten-3-one provided three independent observations of the molecular conformation of this molecule. Polymorph I (mp 114–117 °C) was obtained by bromination of 17β-acetoxy-4-androsten-3-one with *N*-bromosuccimide and by acetylation of 6β-bromo-17β-hydroxy-4-androsten-3-one and consisted of conformers a and b in a 1:1 ratio. Polymorph II (mp 138–141 °C) was obtained by a treatment of polymorph I with chloroform–methanol (9:1) under epimerization condition and consists of one conformer only. Despite differences in solid IR spectra and dissimilarities in crystal packing environment, the three conformers are nearly identical in overall shape. The A rings of the three molecules have 1α-sofa conformations, and the B and C rings have chair conformations. The stacking of the 3-carbonyl groups in polymorph I contributes to denser packing and a shift in carbonyl frequency. The closest contact in the polymorph II involves the acetate carbonyl and is also reflected in a shift in spectra. The structure determinations demonstrate that while crystal packing has very little influence on overall molecular conformation, it does influence solid-state spectra.

Although the initial report[1] of synthesis of 6β-bromotestosterone acetate[2] described crystals of melting point 140–142 °C, repetition of the same procedure in our hands gave only crystals of melting point 114–117 °C. In the course of preparing 6-bromo-substituted androgens for use in affinity labeling of estrogen synthetase, dimorphic forms of 6β-bromotestosterone acetate were isolated.[3] The lower melting polymorph I was obtained by bromination of testosterone acetate and also by acetylation of 6β-bromotestosterone and was repeatedly recrystallized from 95% EtOH. The higher melting point polymorph II was obtained together with 6α-bromotestosterone acetate by epimerization treatment in $CHCl_3$–MeOH and was also repeatedly recrystallized from 95% EtOH. The integrity of each polymorph was maintained through recrystallization unless seeds of the alternate form were added to the solution, in which case the seed form was obtained. If the 95% ethanol solution of either polymorph was passed through a Millipore filter, subsequent recrystallization

(1) C. Djerassi, G. Rosenkranz, J. Romo, S. Kaufman, and J. Pataki, *J. Am. Chem. Soc.*, **72**, 4534 (1950).

(2) Trivial names and abbreviations used in this manuscript are as follows: NBS = *N*-bromosuccimide, testosterone = 17β-hydroxy-4-androsten-3-one, 6β-bromotestosterone = 6β-bromo-17β-hydroxy-4-androsten-3-one, 6β-bromotestosterone acetate = 17β-acetoxy-6β-bromo-4-androsten-3-one.

(3) M. Numazawa and Y. Osawa, *Steroids*, **34**, 347 (1979).

0022-3263/81/1946-2650$01.25/0

Table I. Crystal Data for 6β-Bromotestosterone Acetate ($C_{21}H_{29}O_3Br$, mol wt 409.3)

	I	II
mp, °C	114–117	138–141
a, Å	29.231 (5)	13.404 (2)
b, Å	6.187 (1)	19.544 (3)
c, Å	22.317 (4)	7.725 (1)
β, deg	100.23	90.0
vol, Å^3	3972.0	2023.6
ρ_{calcd}, g/cm^3	1.37	1.34
space group	C_2	$P2_12_12_1$
Z	8	4
cryst size, mm	0.12 × 0.20 × 0.36	0.37 × 0.38 × 0.86
R, % (rflctn measd)	8.4 (3247)	11.9 (2446)
R, % (rflctns above bkgd ($I > 4\sigma I$))	7.9 (2995)	10.4 (1895)

produced the lower melting polymorph. There have been numerous reports of polymorphism of steroidal compounds. However, total structure determination to illuminate the cause has seldom been made. The crystal structures of the two polymorphs of 6β-bromotestosterone acetate were studied in order to compare the molecular conformations and determine, if possible, the cause of differences in the infrared spectra.

Experimental Section

Crystal data for the two polymorphs are given in Table I. The intensities were measured with an Enraf-Nonius CAD-4 diffractometer using nickel-filtered copper radiation without a monochromator. Lorentz and polarization corrections were applied to the data, and the structures were solved by routine application of the heavy-atom method. Although more than half of the hydrogen atoms in each polymorph could be located in Fourier difference maps, efforts to refine the hydrogen atom positional and thermal parameters led to results that were chemically unacceptable. Consequently, the hydrogens were introduced into the refinement with standard geometry and were not allowed to refine. The difference Fourier maps showed no evidence of any solvent in either polymorph. Furthermore, the cell volumes are too small to accommodate solvent. The quantities ($1/\sigma_F^2$) were used to weight the least-squares differences for the observed data, where σ_F was as defined by Stout and Jensen[4] (see eq H14) but with an instability factor of 0.06 (instead of 0.01); data for which $F > 2\sigma_F$ were given zero weight. The final values of the residual, $R = \sum||F_o| - |F_c||/\sum|F_o|$, were 0.079 and 0.104 for polymorphs I and II, respectively. The scattering factors used throughout the refinement were generated from the coefficients given by Cromer and Waber in Table 2.2B.[5] Final positional parameters are listed in Table II.

The bond lengths, valence angles, and torsion angles for the two crystallographically independent molecules in polymorph I are compared in Figure 1; those for conformer II are given in Figure 2. The widest range in a single bond length is the 0.08-Å spread in the C(5)–C(6) bond. The valence angle exhibiting the greatest variation is the O(17)–C(20)–C(21) angle which differs by 10° between conformers Ia and II. The observed thermal motion of the steroid was comparable to that seen in many steroid crystal structures. The observed motion of the D rings and the acetate side chains is compared in Figure 3. The carbonyl oxygen is seen to have its greatest amplitude of motion perpendicular to the plane of the acetate group, a commonly observed motion. There appears to be greatest similarity in the thermal motion of conformers Ib and II, the molecules with nearly identical side-chain orientation. The consistency between the corresponding bond lengths in the conformers and the well-behaved thermal motion indicated that the determination is of sufficient reliability

(4) G. H. Stout and J. H. Jensen, "X-ray Structure Determination", Macmillan, New York, 1968.
(5) D. T. Cromer and J. T. Waber, "International Tables for X-ray Crystallography", Vol. IV, J. A. Iber and W. C. Hamilton, Eds., Kynoch Press, Birmingham, England, 1974, Table 2.2B.

Table II. Atomic Coordinates

atom	X/A	Y/B	Z/C
(a) For Conformers a and b in Crystalline Polymorph I of 17β-Acetoxy-6β-bromo-4-androsten-3-one			
C(1)	0.28135 (26)	0.0483 (19)	0.47178 (37)
C(2)	0.25240 (28)	−0.0296 (19)	0.40962 (42)
C(3)	0.27537 (30)	0.0245 (19)	0.35813 (43)
C(4)	0.32585 (30)	0.0595 (20)	0.36983 (42)
C(5)	0.35271 (28)	0.0381 (17)	0.42491 (36)
C(6)	0.40369 (25)	0.0686 (16)	0.43126 (36)
C(7)	0.42418 (26)	0.1955 (17)	0.48836 (41)
C(8)	0.41157 (26)	0.0927 (0)	0.54570 (36)
C(9)	0.35835 (25)	0.0866 (17)	0.53969 (35)
C(10)	0.33242 (24)	−0.0335 (17)	0.48205 (37)
C(11)	0.34465 (27)	−0.0158 (20)	0.59941 (38)
C(12)	0.36813 (29)	0.1058 (19)	0.65730 (38)
C(13)	0.42127 (30)	0.1040 (19)	0.66125 (38)
C(14)	0.43097 (27)	0.2219 (16)	0.60213 (42)
C(15)	0.48300 (28)	0.2671 (22)	0.61779 (44)
C(16)	0.49214 (30)	0.3219 (21)	0.68687 (47)
C(17)	0.44737 (30)	0.2670 (20)	0.70830 (42)
C(18)	0.44144 (34)	−0.1274 (18)	0.66898 (44)
C(19)	0.33548 (28)	−0.2730 (18)	0.48720 (41)
C(20)	0.46948 (38)	0.2693 (26)	0.81848 (48)
C(21)	0.47685 (51)	0.1042 (33)	0.87078 (54)
BR(6β)	0.43666 (3)	−0.2068 (3)	0.42648 (5)
O(3)	0.25368 (23)	0.0408 (14)	0.30503 (28)
O(17β)	0.45543 (26)	0.1434 (15)	0.76678 (32)
O(20)	0.47440 (29)	0.4500 (17)	0.81861 (35)
C(1′)	0.76170 (30)	0.0007 (23)	0.18390 (45)
C(2′)	0.74273 (31)	0.0489 (23)	0.24391 (47)
C(3′)	0.78048 (33)	0.0438 (19)	0.29832 (46)
C(4′)	0.82789 (30)	0.0762 (17)	0.28949 (40)
C(5′)	0.83879 (30)	0.1336 (19)	0.23581 (43)
C(6′)	0.88999 (29)	0.1798 (24)	0.23341 (38)
C(7′)	0.90606 (29)	0.0949 (23)	0.17735 (44)
C(8′)	0.87125 (29)	0.1558 (19)	0.11848 (40)
C(9′)	0.82359 (28)	0.0618 (19)	0.12164 (39)
C(10′)	0.80176 (27)	0.1462 (19)	0.17681 (41)
C(11′)	0.78893 (31)	0.0868 (22)	0.05996 (43)
C(12′)	0.81051 (34)	0.0134 (23)	0.00477 (44)
C(13′)	0.85626 (29)	0.1129 (21)	0.00241 (39)
C(14′)	0.88953 (30)	0.0655 (20)	0.06338 (42)
C(15′)	0.93627 (35)	0.1258 (28)	0.05261 (48)
C(16′)	0.93494 (39)	0.0579 (35)	−0.01603 (48)
C(17′)	0.88429 (37)	0.0100 (23)	−0.04201 (43)
C(18′)	0.85082 (37)	0.3548 (24)	−0.01060 (46)
C(19′)	0.78608 (33)	0.3842 (20)	0.16617 (44)
C(20′)	0.86023 (36)	−0.0353 (29)	−0.14858 (52)
C(21′)	0.85180 (39)	0.0899 (33)	−0.20710 (47)
BR(6β′)	0.89829 (5)	0.5023 (3)	0.23827 (6)
O(3′)	0.77210 (23)	0.0143 (14)	0.35006 (29)
O(17β′)	0.87267 (29)	0.0997 (16)	−0.10149 (31)
O(20′)	0.85693 (48)	−0.2168 (30)	−0.14215 (43)
(b) For Polymorph II of 17β-Acetoxy-6β-bromo-4-androsten-3-one			
C(1)	0.33431 (60)	0.65703 (50)	0.7364 (13)
C(2)	0.22337 (65)	0.64244 (55)	0.7040 (16)
C(3)	0.19832 (59)	0.65381 (50)	0.5189 (18)
C(4)	0.27393 (66)	0.64348 (45)	0.3914 (16)
C(5)	0.37022 (60)	0.62462 (50)	0.4332 (13)
C(6)	0.44242 (56)	0.61227 (57)	0.2777 (12)
C(7)	0.54705 (57)	0.64160 (43)	0.3227 (10)
C(8)	0.58411 (56)	0.61724 (48)	0.5003 (11)
C(9)	0.51324 (54)	0.64425 (36)	0.6415 (11)
C(10)	0.40381 (55)	0.61337 (51)	0.6229 (12)
C(11)	0.55280 (57)	0.63027 (55)	0.8248 (11)
C(12)	0.66085 (60)	0.65874 (47)	0.8482 (12)
C(13)	0.72945 (55)	0.62961 (44)	0.7147 (11)
C(14)	0.68819 (51)	0.65066 (39)	0.5328 (11)
C(15)	0.77352 (62)	0.63709 (44)	0.4065 (12)
C(16)	0.86939 (62)	0.65093 (43)	0.5165 (15)
C(17)	0.83279 (59)	0.66552 (40)	0.6915 (12)
C(18)	0.74317 (65)	0.55209 (52)	0.7333 (13)
C(19)	0.39645 (66)	0.53946 (55)	0.6691 (14)
C(20)	0.93509 (63)	0.68291 (45)	0.9384 (11)
C(21)	1.00590 (78)	0.65090 (46)	1.0709 (14)
BR(6β)	0.44955 (9)	0.51661 (6)	0.2222 (1)
O(3)	0.11296 (47)	0.67064 (44)	0.4741 (15)
O(17β)	0.90035 (45)	0.64062 (31)	0.8257 (10)
O(20)	0.91879 (78)	0.74207 (34)	0.9340 (11)

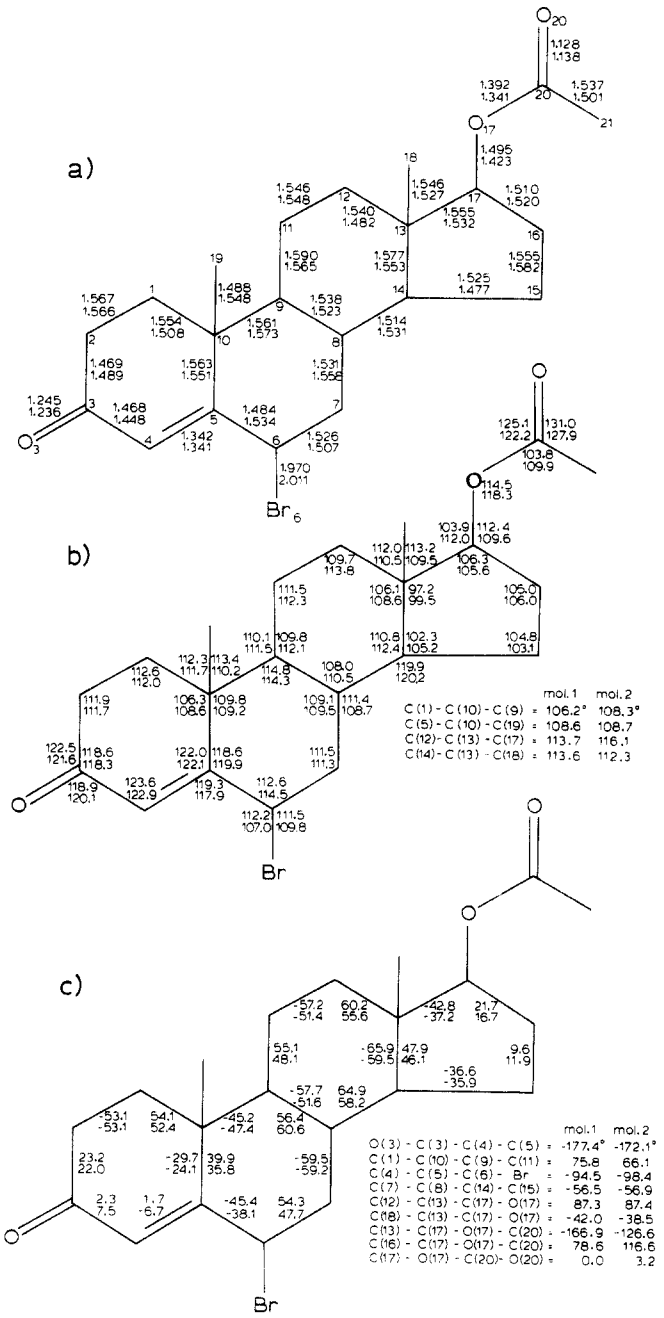

Figure 1. Comparison of (a) bond lengths, (b) valence angles, and (c) torsion angles of conformers Ia and Ib of 6β-bromotestosterone acetate (the top, Ia, molecule 1, and the bottom, Ib, molecule 2). The esd's are 0.011–0.016 Å for bond lengths, 0.5–0.7° for bond angles, and 0.8–1.2° for torsion angles.

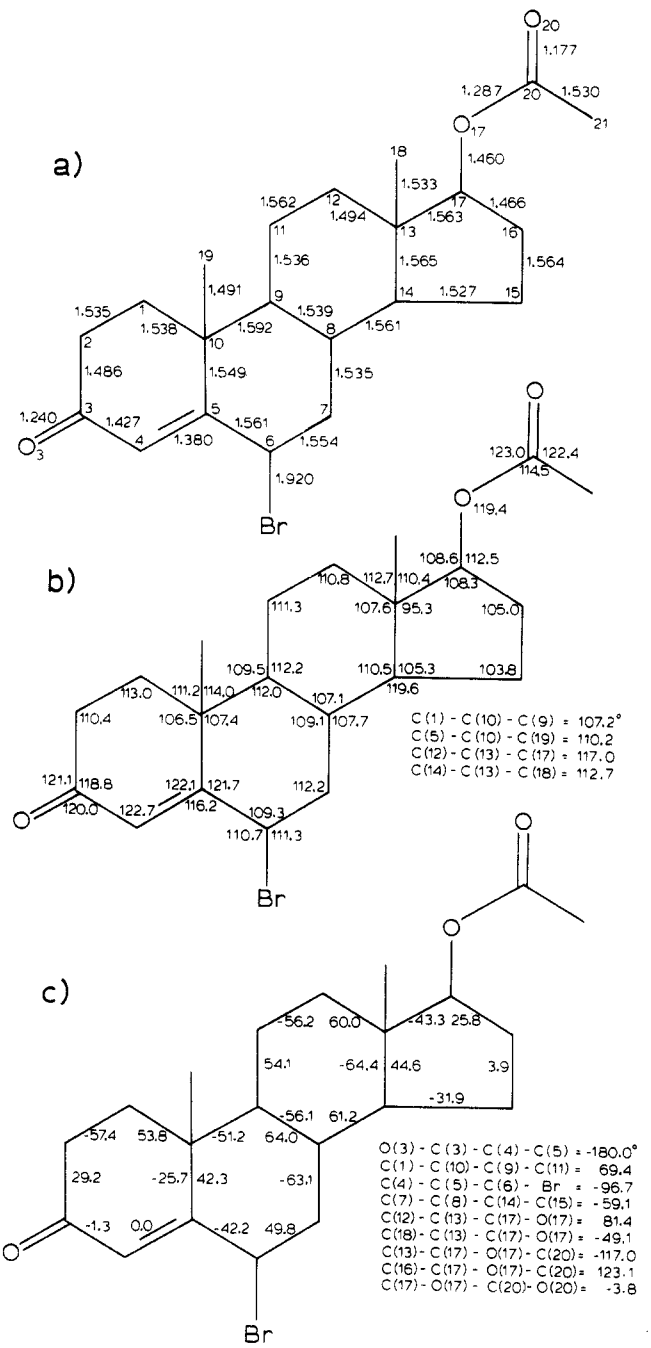

Figure 2. (a)Bond lengths, (b) valence angles, and (c) torsion angles of conformer II of 6β-bromotestosterone acetate. The esd's are 0.011–0.015 Å for bond lengths, 0.6–0.8° for bond angles, and 0.8–1.0° for torsion angles.

to draw the conclusions discussed below.

IR spectra were recorded in a Perkin-Elmer 267 spectrophotometer in a KBr pellet (0.03 w/w %) or $CHCl_3$ (0.2 w/v %). The frequencies of C=O and C=C stretching vibrations were determined by averaging the values of three measurements.

In chloroform solution the spectra of the two polymorphs are indistinguishable (Figure 4a) and have acetate carbonyl, conjugated carbonyl, and C=C stretching frequencies of 1725, 1675, and 1605 cm^{-1}. The solid-state infrared (KBr) spectra for the two polymorphic forms (Figure 4b) differ substantially in the range of 1200–1500 cm^{-1} and very slightly in the carbonyl region. More specifically, the differences in the C–O stretching bands of 17-acetate around 1200–1260 cm^{-1}, the bending vibration of the C(2) methylene group around 1400–1470 cm^{-1},[6] and the C=O and C=C stretching bands at 1730, 1675, and 1605 cm^{-1} (polymorph I) and at 1725, 1672, and 1602 cm^{-1} (polymorph II) were observed. Surprisingly the spectrum of the polymorph having only one molecule in the asymmetric unit appears to be sharper and more detailed. Perhaps the spectrum from the polymorph with two in the asymmetric unit is dampened by averaging.

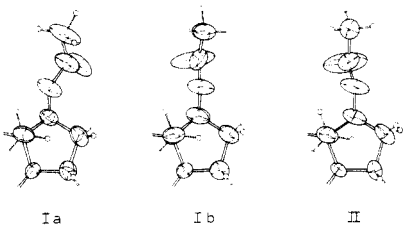

Figure 3. Position 17 side-chain orientations and thermal vibrations of conformers Ib and II are seen to be similar to one another and unlike those observed in conformer Ia.

(6) L. F. Fieser and M. Fieser, "Steroids", Reinhold, New York, 1959, pp 169–175.

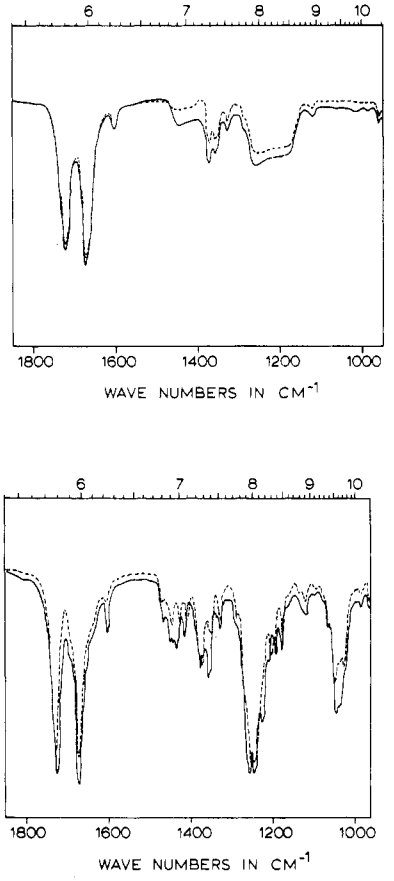

Figure 4. (a) IR spectra of 6β-bromotestosterone acetate in chloroform and (b) IR (KBr) spectra of crystalline polymorphs I (---) and II (—) of 6β-bromotestosterone acetate.

Discussion

Despite significant differences in crystallographic environment, melting point, and solid-state spectra, the three crystallographically independent molecules of 6β-bromotestosterone acetate are found to be nearly identical in overall conformation. The A rings of the three molecules have the 1α-sofa conformation and the B and C rings have chair conformations. A sofa conformation is one in which five of the six atoms in a ring are coplanar and the sixth is out of the plane.

On closer inspection it appears that there is greatest similarity between conformers Ib and II. In Figure 5a conformers Ia and Ib are superimposed by means of a program (FITMOL)[7] that minimizes the separations between corresponding atoms, C(1) through C(17). Similar comparisons between conformer II and conformers Ia and Ib are shown in Figures 5b,c, respectively. Conformers Ia and Ib are seen to differ primarily in the A, C, and D rings and in the 17-acetate orientation. Conformer II is seen to be nearly indistinguishable from conformer Ib. Even the thermal motions of the acetate groups of II and Ib are similar to one another and different from that of Ia (Figure 3). Close examination of Figure 5 reveals that Ia differs from II and Ib by the approximate 6° twist about the length of the steroid. This twist is measured by the pseudo torsion angle C(19)–C(10)–C(13)–C(18) which has values of 15.7°, 8.9°, and 10.1° in conformers Ia, Ib, and II, respectively. The atoms of molecule Ia, which are represented as slightly larger circles in Figures 5a and 5b, are

(7) G. D. Smith, "FITMOL, a Program to Least-Squares Fit Similar Molecules or Molecular Fragments", Medical Foundation of Buffalo, Inc., Buffalo, NY.

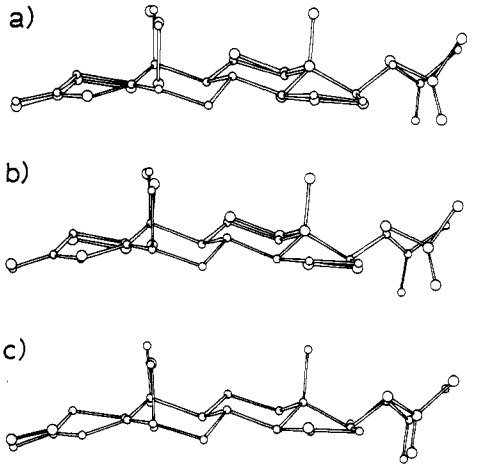

Figure 5. Comparison of conformational isomers of 6β-bromotestosterone acetate using the program FITMOL. Conformer Ia is seen to differ in an identical manner from (a) conformer Ib and (b) conformer II, whereas (c) conformers Ib and II are nearly identical.

seen to be above those of molecules Ib and II at C(11) and C(12) and below those of molecules Ib and II at C(1), C(2), C(15), and C(16). These differences appear to be correlated with the difference in orientation and thermal motion of the 17-acetate side chain.

Although the differences in the conformers are subtle, the crystal environments surrounding each are different (Figure 6). The significant differences in the environments of conformer II relative to conformers Ia and Ib are obvious from Figure 6. Because conformers Ia and Ib are stacked along the *b* cell side, differences in their environment are not as obvious at first glance. However, the central dark molecules in Ia and Ib of Figure 6 are oriented in an identical fashion, illustrating the different pitch of the two molecular stacks and the different environments of the acetate groups. The 3-carbonyl groups of conformers Ia and Ib are stacked over one another with a closest approach of 3.04 Å between O(3) and C(3) of adjacent molecules. This contact promotes denser packing in polymorph I. The calculated densities of polymorphs I and II are 1.37 g/cm^3 and 1.34 g/cm^3, respectively. The closest contact in the high-melting crystals is a 3.30-Å distance from the acetate carbonyl oxygen to C(6) of an adjacent molecule.

Since the conformation of conformer II is nearly identical with that of conformer Ib, the spectra of polymorph I might have been expected to be a composite of the spectra for polymorph II with additional lines due to conformer Ia. The absence of doublets in the carbonyl and C=C regions of the spectra of polymorph I indicates that conformational differences between Ia and Ib are not sufficient enough to be distinguished spectrally. Differences in the carbonyl and C=C stretching frequencies between the polymorphs appear to be related to intermolecular contacts involving the carbonyls. The acetate carbonyl stretching frequency in polymorph II exhibits a −5-cm^{-1} shift relative to the peak in polymorph I. This shift in polymorph II and the difference in the C–O stretching bands may be correlated with the 3.30-Å contact between the acetate carbonyl oxygen and C(6) of an adjacent molecule and with the expansion of the C(17)–C(20)–C(21) angle. The closest contact involving O(20) in polymorph I is 3.55 Å. The 3-carbonyl and C=C frequencies found in polymorph I exhibit a 3-cm^{-1} shift relative to the corresponding peaks in polymorph II, and the bending vibration bands of the C(2) methylene group in the solid spectra show a marked difference. These may

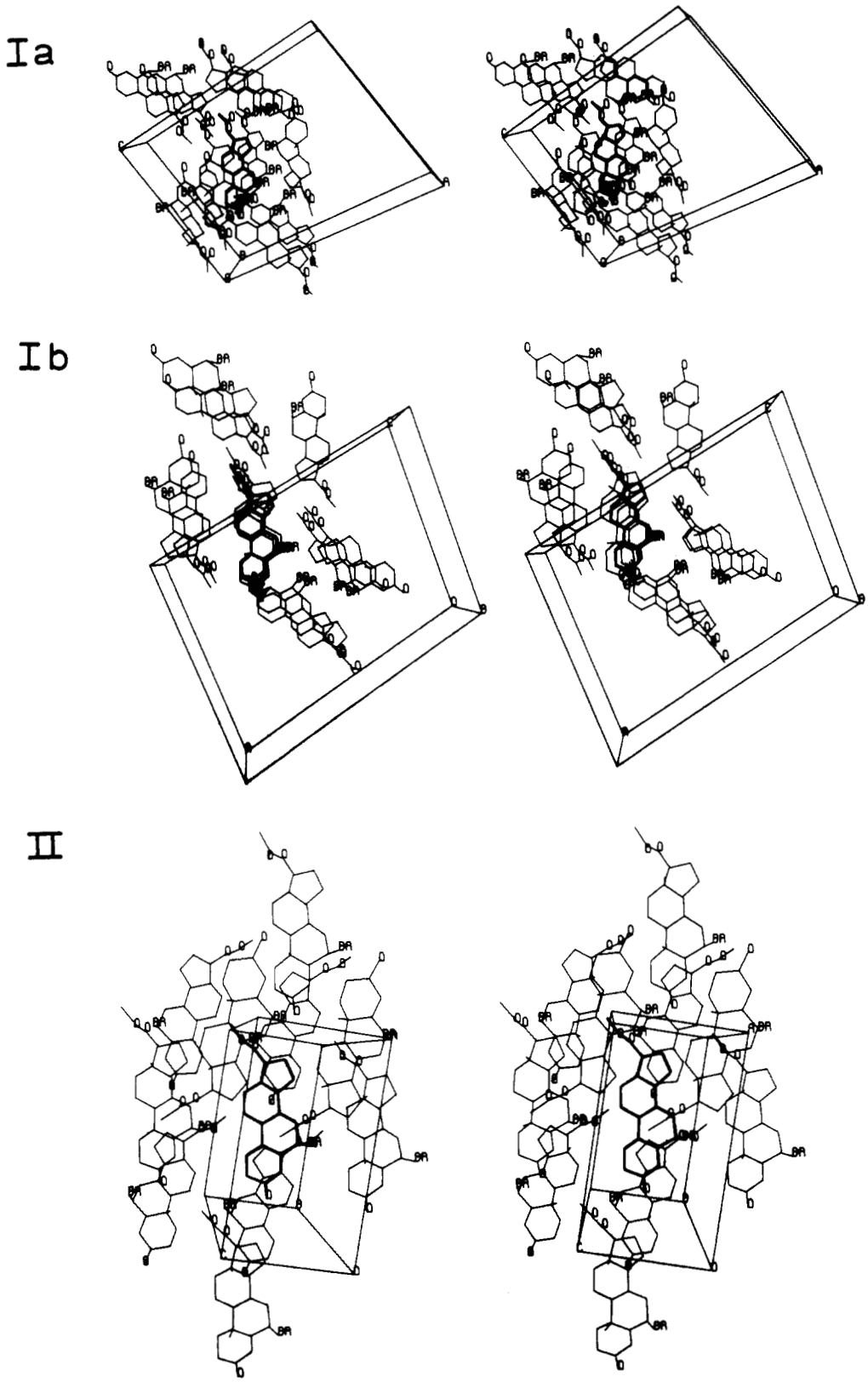

Figure 6. Stereodiagrams reveal the dissimilarity of the immediate environment of the three conformers.

be a consequence of stacking interactions between O(3) and C(3) of 3.04 Å in polymorph I. The C(2) atom of molecule Ia is 3.21 Å from the O(3) atom of molecule Ib.

The greatest differences in solid IR spectra of the two polymorphs occur in the 1300–1500-cm^{-1} region (Figure 4). Since there are no dramatic differences in overall conformation, these variations must be due to subtle differences in intramolecular geometry or intermolecular interactions.

Crystal packing forces are generally believed to have a significant influence upon molecular conformation. At least in the case of polymorphic crystal forms of 17β-acetoxy-6β-bromo-4-androsten-3-one described here, intermolecular interactions have had little influence on overall conformation. Consequently, caution should be exercised when drawing conclusions about the influence of crystal packing, and further careful studies of more flexible molecules in polymorphic forms should be un-

dertaken.

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Registry No. 6β-Bromotestosterone acetate, 1458-93-1.

Preparation of a 6α-Substituted Optically Pure Steroid with Thiophene as the A Ring via Asymmetric Induction. A Circular Dichroism Study†

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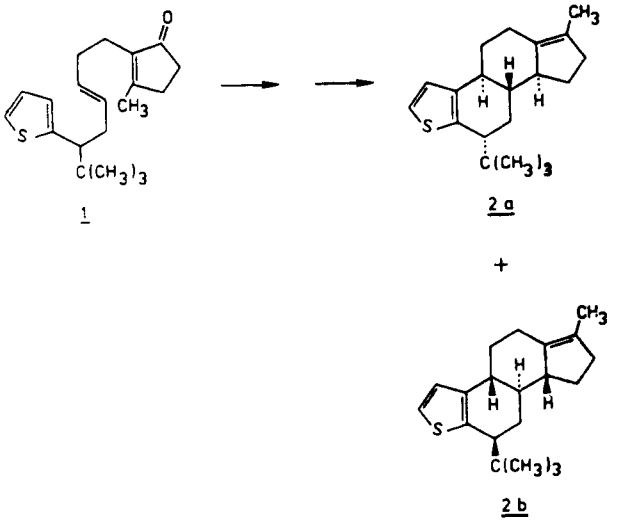
A number of asymmetrically induced cyclization reactions are described, furnishing specifically substituted steroid-like systems with thiophene as the A ring. Ring closure of achiral compounds gives two enantiomeric trans-anti-fused products, containing three chiral carbon atoms each. The presence of a nonepimerizable chirality in the cyclization precursor favors production of one ring-closed diastereomer over the other. A comparable example of an in vivo ring closure is found in the conversion of 2,3-epoxysqualene to various steroids. A chiral center far removed from the cyclization initiator also influences the stereochemical outcome of such cyclizations. A deuterium at *pro*-C-6 (steroid numbering) causes no measurable asymmetrically induced ring closure because of the deuterium's comparable size to a hydrogen atom. A methyl group at *pro*-C-6, however, will cause ring closure to proceed in 97% yield to a 6α-substituted steroid. A 100% asymmetrically induced ring closure in favor of the 6α-substituted products is brought about by a *t*-Bu group. Aforementioned stereospecificities are believed to stem from 1,3-diaxial interactions between the substituent at the chiral carbon atom and the *pro*-C-8 and *pro*-C-10 hydrogen atoms. This gives rise to a model description of the ring closure in terms of "precoiling". The ring closure of the optically pure *tert*-butyl-substituted alkene gives an optically pure steroid, since the reaction proceeds with 100% asymmetric induction. Hereby, a significant yield increase is observed (50% → 80%). The absolute configurations of the precursors and the cyclized products are determined by circular dichroism.

Cyclization of chiral olefins offers an excellent method for the preparation of substituted optically active steroids provided that a high degree of asymmetric induction is operative. A *pro*-C-6 substituted optically pure substrate can afford in principle the 6α,9α and the 6α,9β trans-anti-fused tetracycles or their mirror images, depending on the configuration of the substrate used. The asymmetric induction on the stereochemical outcome of the cyclization favors to a certain amount the formation of one of the two products. Recently, the cyclization of racemic **1** has been described (see Scheme I).[1] Only one racemate, **2a** and **2b**, was formed, demonstrating the ring closure to proceed with 100% asymmetric induction. The cyclization of optically pure **1** thus leads to an optically pure 6α-substituted steroid (vide infra). In order to obtain additional information about the absolute configuration of the steroid, the absolute configuration of **1** was determined.

Scheme I. Cyclization of a *pro*-C-6 *tert*-Butyl-Substituted Steroid Precursor Proceeding with 100% Asymmetric Induction (2a)



Results and Discussion

Resolution and Absolute Configuration of the *pro*-C-6 *tert*-Butyl-Substituted Precursor. Resolution of the Optical Isomers. The method most generally used for separating enantiomers entails the separation of diastereomeric forms. To this effect, the racemic pair is derivatized into two diastereomers which can then be separated by virtue of differences in physical properties. The usual separation methods may vary from pure classical methods such as differences in boiling points and differences in solubilities of a crystalline mixture to chromatographic adsorptions and gas chromatographic retention times. Resolutions were performed on the acids **3**–**5** (see Scheme II). Acid **3** is a precursor of **1** and has the advantage that racemizations are precluded during the en-

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(1) (a) Macco, A. A.; de Brouwer, R. J.; Buck, H. M. *J. Org. Chem.* 1977, *42*, 3196. (b) Macco, A. A.; de Brouwer, R. J.; Nossin, M. M. P.; Godefroi, E. F.; Buck, H. M. *Ibid.* 1978, *43*, 1591.

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