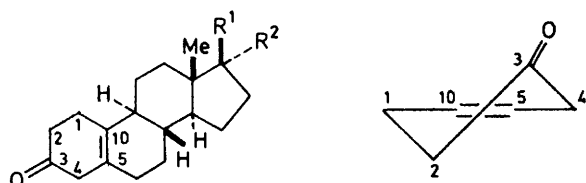


Conformational Preference of Ring A in 3-Oxo- $\Delta^{5,10}$ -steroids: X-Ray Crystal Structure Analysis of 17 α -Ethynyl-17 β -hydroxyestr-5(10)-en-3-one (Norethynodrel)

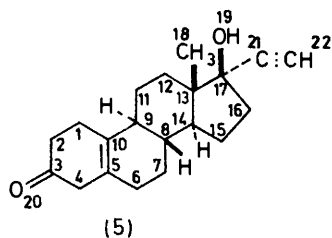
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The crystal structure and solid-state conformations of the title compound (5) have been established by X-ray analysis. Crystals are orthorhombic, space group $P2_12_12_1$, with $a = 21.593(13)$, $b = 22.075(13)$, $c = 7.015(8)$ Å, $Z = 8$. The structure was solved by direct methods and refined by least-squares calculations to R 0.046 over 2 572 statistically significant reflections from diffractometer measurements. The A rings in the two crystallographically independent molecules approximate to envelope conformations in which C(2) is displaced to the α -side in one and to the β -side in the other. Stabilization of the higher energy C(2) β -side envelope form is a consequence of the intramolecular hydrogen bonding arrangement in the crystal. The B ring shapes also differ slightly owing to conformational transmission effects.

BEFORE recent X-ray structural investigations on 17 β -hydroxyestr-5(10)-en-3-one¹ (1) and its iodoacetate derivative (2),² it was held that ring A of 3-oxo- $\Delta^{5,10}$ -steroids would preferentially adopt a half-chair conformation similar to that encountered in cyclohexene (4). Indeed, not only was such a conformation predicted from strain-energy minimization calculations³ on estr-5(10)-en-3-one (3) but also these calculations indicated that the conformer with the carbonyl group displaced in the β -direction and C(2) displaced to the α -side was the more stable by 0.9 kcal mol⁻¹. The X-ray studies,



- (1) $R^1 = \text{OH}, R^2 = \text{H}$
 (2) $R^1 = \text{O}\cdot\text{CO}\cdot\text{CH}_2\text{I}, R^2 = \text{H}$
 (3) $R^1 = R^2 = \text{H}$



however, clearly showed that in both compounds examined ring A consistently approximates to an envelope (diplanar, sofa, semiplanar) form with only C(2) displaced significantly from the C(1),C(4)—(6),C(9),C(10) least-squares plane and in the α -direction. We here report a single-crystal X-ray analysis of

another representative of this class, 17 α -ethynyl-17 β -hydroxyestr-5(10)-en-3-one (5). The results are of particular significance with respect to this conformational problem as they reveal that the two molecules comprising the asymmetric crystal unit approximate to different ring A envelope forms in which C(2) is displaced to the α -side in one molecule and to the β -side in the other.

EXPERIMENTAL

Crystal Data.— $\text{C}_{20}\text{H}_{26}\text{O}_2$, $M = 298.4$. Orthorhombic, $a = 21.593(13)$, $b = 22.075(13)$, $c = 7.015(8)$ Å, $U = 3\ 343$ Å³, D_m (floatation) = 1.19, $Z = 8$, $D_c = 1.186$ g cm⁻³, $F(000) = 1\ 296$, Mo- K_α radiation, $\lambda = 0.710\ 7$ Å, Cu- K_α radiation, $\lambda = 1.541\ 8$ Å; $\mu(\text{Mo-}K_\alpha) = 0.81$ cm⁻¹, $\mu(\text{Cu-}K_\alpha) = 5.89$ cm⁻¹. Space group $P2_12_12_1$ (D_2^2) from systematic absences: $h00$ when $h \neq 2n$, $0k0$ when $k \neq 2n$, $00l$ when $l \neq 2n$.

Crystallographic Analysis.—Preliminary unit-cell dimensions obtained from precession photographs taken with Mo- K_α radiation were refined by least-squares treatment of the θ , χ , and ϕ angles for 26 reflections from a crystal of dimensions ca. 0.40 × 0.40 × 0.40 mm oriented on a glass fibre to rotate with the crystal c axis parallel to the ϕ axis of an Enraf-Nonius CAD 3 automated diffractometer (Mo- K_α radiation; 3° take-off angle). Two sets of intensity data were recorded by use of the θ — 2θ scanning technique as described previously⁴ with scanwidths ($0.90 + 0.45 \tan \theta$)°. One data set, to θ 25°, was recorded with Mo- K_α radiation and subsequently a second set was recorded from the same crystal with Cu- K_α radiation. The usual Lorentz and polarization corrections were applied to 1 361 (Mo- K_α data) and 2 572 (Cu- K_α data) statistically significant [$I > 2.0\sigma(I)$, where $\sigma^2(I) = \text{scan count} + \text{total background count}$] reflections which were used in the structure determination and refinement.

Structure Analysis.—The structure was solved by direct non-centrosymmetric phase-determining procedures using the Mo- K_α data set. A number of early attempts in 1971 to solve the phase problem by the symbolic addition procedure and tangent-formula refinement⁵ on 473 phases

¹ R. R. Sobti, S. G. Levine, and J. Bordner, *Acta Cryst.*, 1972, **B28**, 2292.

² J. Bordner, R. R. Sobti, and S. G. Levine, *J. Amer. Chem. Soc.*, 1971, **93**, 5588.

³ N. C. Cohen, *Tetrahedron*, 1971, **27**, 789.

⁴ D. L. McFadden and A. T. McPhail, *J.C.S. Dalton*, 1974, 363.

⁵ For the approach used see e.g. P. A. Luhan and A. T. McPhail, *J.C.S. Perkin II*, 1973, 51.

having $|E| > 1.30$ failed to yield any E maps with recognizable molecular features. The principal reason for these

TABLE 1

Fractional atomic co-ordinates ($\times 10^4$) for the non-hydrogen atoms, with estimated standard deviations in parentheses

Atom	x	y	z
C(1)	123(2)	7 589(2)	2 166(7)
C(2)	507(2)	8 174(2)	2 172(7)
C(3)	162(2)	8 691(2)	2 997(7)
C(4)	-188(2)	8 578(2)	4 771(6)
C(5)	-348(2)	7 926(1)	5 199(6)
C(6)	-692(2)	7 847(2)	7 026(7)
C(7)	-100(2)	7 228(2)	7 254(6)
C(8)	-594(2)	6 723(1)	6 476(6)
C(9)	-458(2)	6 833(1)	4 353(6)
C(10)	-215(2)	7 474(2)	4 000(6)
C(11)	-53(2)	6 322(2)	3 525(6)
C(12)	-353(2)	5 701(2)	3 813(6)
C(13)	-497(2)	5 581(2)	5 913(6)
C(14)	-899(2)	6 102(1)	6 694(6)
C(15)	-1 110(2)	5 883(2)	8 655(7)
C(16)	-1 160(2)	5 178(2)	8 411(7)
C(17)	-938(2)	5 044(2)	6 368(7)
C(18)	105(2)	5 487(2)	7 042(8)
O(19)	-648(1)	4 456(1)	6 346(5)
O(20)	163(1)	9 190(1)	2 247(5)
C(21)	-1 467(2)	5 033(2)	5 037(8)
C(22)	-1 895(3)	5 035(2)	4 003(11)
C(1')	7 169(2)	507(2)	936(7)
C(2')	6 660(2)	51(2)	1 336(8)
C(3')	6 496(2)	-286(2)	-425(8)
C(4')	6 317(2)	100(2)	-2 058(8)
C(5')	6 634(2)	715(2)	-2 145(6)
C(6')	6 466(2)	1 085(2)	-3 838(7)
C(7')	6 631(2)	1 754(2)	-3 582(7)
C(8')	7 285(2)	1 810(2)	-2 841(6)
C(9')	7 339(2)	1 519(2)	-872(6)
C(10')	7 032(2)	895(1)	-805(6)
C(11')	8 018(2)	1 527(2)	-179(7)
C(12')	8 272(2)	2 181(2)	-313(7)
C(13')	8 198(2)	2 500(2)	-2 028(6)
C(14')	7 513(2)	2 460(2)	-2 654(5)
C(15')	7 468(2)	2 895(2)	-4 365(7)
C(16')	7 932(2)	3 398(2)	-3 893(7)
C(17')	8 283(2)	3 202(2)	-2 056(7)
C(18')	8 639(2)	2 222(2)	-3 499(8)
O(19')	8 925(1)	3 355(1)	-2 109(5)
O(20')	6 511(2)	-836(1)	-565(7)
C(21')	7 997(2)	3 486(2)	-367(7)
C(22')	7 781(3)	3 732(2)	959(9)

failures was the limitations in the number of unknown starting symbols which our programme could accept. At a later date the more powerful MULTAN⁶ programme became available to us and use of this led to successful solution of the phase problem. With the input data set restricted to 250 $|E|$ values > 1.53 and allowing the programme to select four starting reflections in addition to three origin-defining reflections, the programme produced a set of phase angles which allowed the positions of major portions of the two crystallographically independent molecules to be located in an E map. Positions for the remaining non-hydrogen atoms were obtained from a weighted F_o Fourier synthesis phased by these partial structures.

Full-matrix least-squares adjustment of carbon and oxygen positional and thermal parameters, at first iso-

tropic and subsequently anisotropic, and with hydrogen atoms included at their calculated positions in the later stages, proceeded smoothly to convergence at R 0.066. In order to increase the number of observations and thereby permit adjustment of the hydrogen atom positional and isotropic thermal parameters the intensity data were re-collected with Cu- K_α radiation. Further least-squares refinement converged at R 0.046 for the Cu- K_α data set. Final positional parameters for the carbon and oxygen atoms are in Table 1. Hydrogen atom positions, isotropic

TABLE 2

Hydrogen atom fractional co-ordinates ($\times 10^3$), isotropic thermal parameters, and distances ($d/\text{\AA}$) to their bonded carbon or oxygen atoms; estimated standard deviations are in parentheses

Atom	x	y	z	$B/\text{\AA}^2$	$d/\text{\AA}$
H(1 α)	-20(2)	764(2)	104(7)	6.1(11)	1.06(5)
H(1 β)	40(2)	720(2)	176(7)	5.0(10)	1.07(4)
H(2 α)	66(2)	825(2)	89(6)	3.5(9)	0.97(4)
H(2 β)	89(2)	807(2)	317(6)	4.0(9)	1.12(4)
H(4 α)	-57(2)	884(2)	479(6)	4.0(9)	1.01(4)
H(4 β)	8(2)	873(2)	576(7)	5.2(10)	0.95(4)
H(6 α)	-104(2)	820(2)	726(6)	4.8(9)	1.09(4)
H(6 β)	-45(2)	792(2)	805(7)	4.9(10)	0.91(4)
H(7 α)	-145(2)	718(2)	644(6)	3.5(8)	1.12(4)
H(7 β)	-110(2)	715(2)	861(5)	3.2(8)	0.99(4)
H(8)	-19(2)	670(2)	730(6)	3.4(8)	1.05(4)
H(9)	-88(1)	686(1)	369(5)	2.7(7)	1.02(3)
H(11 α)	3(2)	638(2)	221(7)	5.2(10)	0.95(5)
H(11 β)	41(2)	632(2)	406(7)	5.1(11)	1.06(5)
H(12 α)	-75(2)	577(2)	301(6)	4.3(9)	1.04(4)
H(12 β)	-12(2)	536(2)	324(6)	4.5(10)	1.00(4)
H(14)	-127(2)	608(1)	587(5)	2.6(7)	0.99(3)
H(15 α)	-153(2)	603(2)	899(5)	2.5(7)	0.99(3)
H(15 β)	-78(2)	597(1)	963(6)	3.9(9)	1.01(4)
H(16 α)	-160(2)	502(2)	855(7)	4.8(10)	1.01(4)
H(16 β)	-87(2)	497(2)	931(7)	5.1(10)	1.01(4)
H(18 α)	35(2)	587(2)	668(6)	4.3(9)	1.05(5)
H(18 β)	7(2)	540(2)	840(6)	5.3(11)	0.97(5)
H(18 γ)	34(2)	512(2)	634(7)	5.9(11)	1.08(5)
H(19)	-62(3)	422(3)	527(11)	11.8(22)	0.92(7)
H(22)	-222(2)	506(3)	318(9)	8.9(15)	0.92(5)
H(1' α)	756(2)	26(2)	77(7)	6.6(12)	1.00(5)
H(1' β)	720(2)	80(2)	205(6)	4.0(9)	1.01(4)
H(2' α)	623(2)	25(2)	194(7)	6.3(11)	1.11(5)
H(2' β)	679(2)	-18(2)	238(6)	3.8(9)	0.94(4)
H(4' α)	584(1)	17(2)	-201(7)	5.1(10)	1.04(4)
H(4' β)	637(1)	-11(1)	-317(5)	2.3(7)	0.92(4)
H(6' α)	603(2)	101(2)	-425(6)	3.4(8)	1.00(4)
H(6' β)	669(2)	93(2)	-494(6)	4.1(9)	0.97(4)
H(7' α)	635(2)	195(2)	-256(6)	3.8(9)	1.04(4)
H(7' β)	662(2)	195(2)	-475(6)	3.2(8)	0.93(4)
H(8')	754(2)	161(1)	-363(5)	2.4(7)	0.90(3)
H(9')	711(1)	180(1)	1(5)	2.0(7)	1.00(3)
H(11' α)	805(2)	135(2)	105(6)	3.8(9)	0.95(4)
H(11' β)	826(2)	123(2)	-116(6)	4.4(9)	1.09(4)
H(12' α)	801(2)	236(2)	83(6)	3.6(9)	0.97(4)
H(12' β)	871(2)	215(2)	17(6)	4.2(9)	0.96(4)
H(14')	727(1)	268(1)	-161(5)	2.1(7)	1.02(3)
H(15' α)	704(2)	303(2)	-462(7)	5.8(11)	1.00(4)
H(15' β)	756(2)	273(2)	-551(7)	6.4(11)	0.90(5)
H(16' α)	770(2)	382(2)	-363(6)	3.6(8)	1.08(4)
H(16' β)	823(2)	341(2)	-497(7)	5.6(10)	0.99(5)
H(18' α)	855(2)	176(2)	-363(8)	6.9(12)	1.05(5)
H(18' β)	861(2)	240(2)	-466(8)	7.2(12)	0.91(5)
H(18' γ)	907(3)	224(3)	-304(11)	8.5(18)	0.99(6)
H(19')	893(3)	376(3)	-253(10)	11.1(19)	0.94(6)
H(22')	759(2)	391(2)	217(8)	8.2(13)	1.03(5)

thermal parameters, and distances to their bonded atoms are in Table 2. Tables of anisotropic temperature factor

⁶ G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

parameters, valency angles involving hydrogen atoms, and a listing of the observed and calculated structure amplitudes

TABLE 3

Interatomic distances (Å) and angles (°) involving non-hydrogen atoms, with estimated standard deviations in parentheses

	Unprimed	Primed
(a) Bond lengths		
C(1)-C(2)	1.535(5)	1.518(7)
C(1)-C(10)	1.500(6)	1.521(6)
C(2)-C(3)	1.481(5)	1.484(7)
C(3)-C(4)	1.477(6)	1.478(7)
C(3)-O(20)	1.221(5)	1.220(5)
C(4)-C(5)	1.510(5)	1.522(5)
C(5)-C(6)	1.491(6)	1.486(6)
C(5)-C(10)	1.336(5)	1.334(6)
C(6)-C(7)	1.531(5)	1.530(5)
C(7)-C(8)	1.524(5)	1.509(5)
C(8)-C(9)	1.537(6)	1.528(6)
C(8)-C(14)	1.529(5)	1.523(5)
C(9)-C(10)	1.529(5)	1.529(5)
C(9)-C(11)	1.540(5)	1.545(6)
C(11)-C(12)	1.531(5)	1.545(5)
C(12)-C(13)	1.529(6)	1.514(6)
C(13)-C(14)	1.543(5)	1.545(5)
C(13)-C(17)	1.553(5)	1.561(5)
C(13)-C(18)	1.537(6)	1.533(6)
C(14)-C(15)	1.527(6)	1.540(6)
C(15)-C(16)	1.570(5)	1.533(6)
C(16)-C(17)	1.540(7)	1.557(6)
C(17)-O(19)	1.439(4)	1.428(4)
C(17)-C(21)	1.476(6)	1.476(6)
C(21)-C(22)	1.175(8)	1.174(8)
(b) Valency angles		
C(2)-C(1)-C(10)	113.7(3)	112.4(4)
C(1)-C(2)-C(3)	112.2(3)	110.5(4)
C(2)-C(3)-C(4)	117.2(3)	114.8(3)
C(2)-C(3)-O(20)	121.7(4)	124.0(5)
C(4)-C(3)-O(20)	121.1(4)	121.2(5)
C(3)-C(4)-C(5)	116.4(3)	115.3(4)
C(4)-C(5)-C(6)	113.3(3)	114.4(4)
C(4)-C(5)-C(10)	122.5(3)	121.8(4)
C(6)-C(5)-C(10)	124.1(3)	123.8(3)
C(5)-C(6)-C(7)	114.4(3)	112.4(4)
C(6)-C(7)-C(8)	111.2(3)	109.6(3)
C(7)-C(8)-C(9)	110.0(3)	110.4(3)
C(7)-C(8)-C(14)	111.7(3)	114.1(3)
C(9)-C(8)-C(14)	108.7(3)	107.0(3)
C(8)-C(9)-C(10)	111.6(3)	111.9(3)
C(8)-C(9)-C(11)	111.0(3)	110.7(3)
C(10)-C(9)-C(11)	115.0(3)	114.3(3)
C(1)-C(10)-C(5)	121.2(3)	121.6(3)
C(1)-C(10)-C(9)	117.5(3)	116.6(3)
C(5)-C(10)-C(9)	121.1(3)	121.7(4)
C(9)-C(11)-C(12)	111.5(3)	110.7(3)
C(11)-C(12)-C(13)	111.6(3)	112.2(3)
C(12)-C(13)-C(14)	109.1(3)	109.0(3)
C(12)-C(13)-C(17)	117.1(3)	117.4(3)
C(12)-C(13)-C(18)	110.3(3)	109.9(3)
C(14)-C(13)-C(17)	98.8(3)	99.6(3)
C(14)-C(13)-C(18)	113.2(3)	112.4(3)
C(17)-C(13)-C(18)	108.1(3)	108.3(3)
C(8)-C(14)-C(13)	113.0(3)	112.8(3)
C(8)-C(14)-C(15)	120.2(3)	119.9(3)
C(13)-C(14)-C(15)	104.5(3)	104.3(3)
C(14)-C(15)-C(16)	103.7(3)	104.0(4)
C(15)-C(16)-C(17)	105.7(3)	107.2(3)
C(13)-C(17)-C(16)	103.6(3)	103.3(3)
C(13)-C(17)-O(19)	114.8(3)	110.5(3)
C(13)-C(17)-C(21)	110.9(3)	111.2(3)
C(16)-C(17)-O(19)	108.9(3)	112.7(3)
C(16)-C(17)-C(21)	110.5(4)	110.0(3)
O(19)-C(17)-C(21)	108.4(3)	109.1(3)
C(17)-C(21)-C(22)	178.4(5)	177.4(5)

TABLE 3 (Continued)

(c) Intermolecular separations ≤ 3.65 Å			
O(20) ... O(19 ^I)	2.79	O(20) ... C(17 ^I)	3.57
O(19) ... O(19 ^{III})	2.82	O(19') ... C(3 ^{II})	3.57
O(19') ... C(4 ^{II})	3.22	C(3) ... O(19 ^I)	3.64
O(20') ... C(18 ^{IV})	3.40	O(20) ... C(6 ^V)	3.65
O(20) ... C(12 ^I)	3.44	C(22') ... C(22 ^{VI})	3.65
O(19') ... C(5 ^{II})	3.48		

Roman numeral superscripts refer to the following transformations of the co-ordinates in Table 1:

I	$-x, \frac{1}{2} + y, \frac{1}{2} - z$	IV	$\frac{3}{2} - x, -y, \frac{1}{2} + z$
II	$1 - x, -\frac{1}{2} + y, \frac{1}{2} - z$	V	$\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$
III	$-1 + x, y, 1 + z$	VI	$1 + x, y, z$

TABLE 4

Torsion angles (°); the angle A-B-C-D is defined as positive if, when viewed along the B-C bond, atom A must be rotated clockwise to eclipse atom D

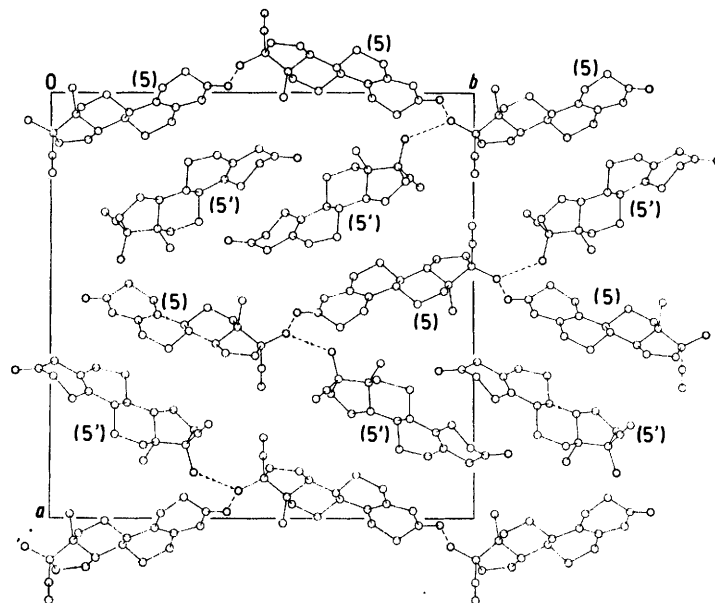
	Unprimed	Primed
C(10)-C(1)-C(2)-C(3)	-44.7	49.2
C(2)-C(1)-C(10)-C(5)	22.6	-21.4
C(2)-C(1)-C(10)-C(9)	-163.3	154.7
C(1)-C(2)-C(3)-C(4)	44.3	-55.4
C(1)-C(2)-C(3)-O(20)	-135.4	123.8
C(2)-C(3)-C(4)-C(5)	-20.6	31.6
O(20)-C(3)-C(4)-C(5)	159.1	-147.7
C(3)-C(4)-C(5)-C(6)	179.1	177.7
C(3)-C(4)-C(5)-C(10)	-3.9	-1.7
C(4)-C(5)-C(6)-C(7)	165.0	162.8
C(10)-C(5)-C(6)-C(7)	-12.0	-17.8
C(4)-C(5)-C(10)-C(1)	2.2	-2.9
C(4)-C(5)-C(10)-C(9)	-171.8	-178.7
C(6)-C(5)-C(10)-C(1)	178.9	177.8
C(6)-C(5)-C(10)-C(9)	4.9	2.0
C(5)-C(6)-C(7)-C(8)	39.0	47.7
C(6)-C(7)-C(8)-C(9)	-59.1	-63.1
C(6)-C(7)-C(8)-C(14)	-180.0	176.3
C(7)-C(8)-C(9)-C(10)	51.2	46.5
C(7)-C(8)-C(9)-C(11)	-179.1	175.3
C(14)-C(8)-C(9)-C(10)	173.9	171.3
C(14)-C(8)-C(9)-C(11)	-56.5	-60.0
C(7)-C(8)-C(14)-C(13)	179.9	-176.0
C(7)-C(8)-C(14)-C(15)	-55.9	-52.5
C(9)-C(8)-C(14)-C(13)	58.2	61.6
C(9)-C(8)-C(14)-C(15)	-177.6	-175.0
C(8)-C(9)-C(10)-C(1)	161.0	167.7
C(8)-C(9)-C(10)-C(5)	-24.8	-16.3
C(11)-C(9)-C(10)-C(1)	33.5	40.9
C(11)-C(9)-C(10)-C(5)	-152.3	-143.1
C(8)-C(9)-C(11)-C(12)	56.4	57.5
C(10)-C(9)-C(11)-C(12)	-176.8	-175.1
C(9)-C(11)-C(12)-C(13)	-55.8	-54.2
C(11)-C(12)-C(13)-C(14)	54.9	53.4
C(11)-C(12)-C(13)-C(17)	165.9	165.5
C(11)-C(12)-C(13)-C(18)	-70.0	-70.1
C(12)-C(13)-C(14)-C(8)	-57.5	-58.6
C(12)-C(13)-C(14)-C(15)	170.1	169.6
C(17)-C(13)-C(14)-C(8)	179.8	177.9
C(17)-C(13)-C(14)-C(15)	47.4	46.2
C(18)-C(13)-C(14)-C(8)	65.8	63.4
C(18)-C(13)-C(14)-C(15)	-66.6	-68.3
C(12)-C(13)-C(17)-C(16)	-161.2	-158.4
C(12)-C(13)-C(17)-O(19)	80.3	80.9
C(12)-C(13)-C(17)-C(21)	-42.7	-40.5
C(14)-C(13)-C(17)-C(16)	-44.5	-41.1
C(14)-C(13)-C(17)-O(19)	-162.9	-161.8
C(14)-C(13)-C(17)-C(21)	74.1	76.9
C(18)-C(13)-C(17)-C(16)	73.5	76.5
C(18)-C(13)-C(17)-O(19)	-44.7	-44.2
C(18)-C(13)-C(17)-C(21)	-167.9	-165.6
C(8)-C(14)-C(15)-C(16)	-160.0	-160.5
C(13)-C(14)-C(15)-C(16)	-31.8	-33.1
C(14)-C(15)-C(16)-C(17)	3.3	6.4
C(15)-C(16)-C(17)-C(13)	26.0	22.0
C(15)-C(16)-C(17)-O(19)	148.5	141.2
C(15)-C(16)-C(17)-C(21)	-92.8	-96.8

for the Cu- K_{α} data set are deposited in Supplementary Publication No. SUP 21839 (23 pp., 1 microfiche).*

In all the structure-factor calculations, scattering factors for carbon and oxygen were taken from ref. 7, and for hydrogen from ref. 8. In the least-squares calculations $\Sigma w\Delta^2$ was minimized, with weights w given by $\sqrt{w} = 1$ for $|F_o| \leq 16.0$ and $\sqrt{w} = 16.0/|F_o|$ for $|F_o| > 16.0$.

RESULTS AND DISCUSSION

Interatomic distances, valency and torsion angles involving the non-hydrogen atoms are in Tables 3 and 4.



Arrangement of (5) and (5') molecules in the crystal, viewed in projection along the c axis; hydrogen bonds are denoted by broken lines

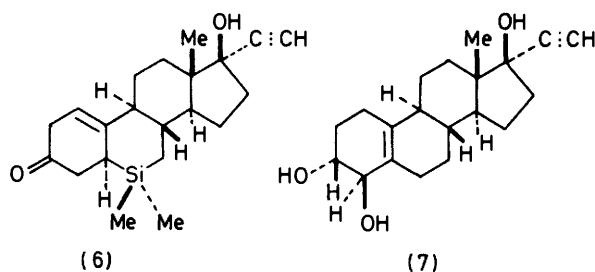
The arrangement of the two crystallographically independent molecules in the crystal is illustrated in the Figure; they are designated (5) and (5'). The shortest intermolecular separations occur between the hydroxy-groups of adjacent (5) and (5') molecules [$O(19) \cdots O(19')$ 2.82, $O(19) \cdots H(19')$ 1.95 Å] and between the hydroxy-group of the reference molecule (5) and the carbonyl oxygen atom of another (5) molecule related by the 2_1 screw axis along the b direction [$O(19) \cdots O(20)$ 2.79, $H(19) \cdots O(20)$ 2.03 Å]; both of these are typical of hydrogen bonds. All other short intermolecular separations correspond to normal van der Waals type interactions.

Endocyclic torsion angles defining the conformations of the β,γ -cyclohexenone A rings in compounds (1), (5), (5'), and (6),⁹ and the cyclohexene B rings in compounds (1), (5), (5'), and (7),¹⁰ and the sums of their deviations from ideal half-chair ($C_2 - HC$) and envelope ($C_s - E$) symmetry-constrained values are presented in Table 5. Although the consistently small ring $A \omega_4$ and ω_5 torsion

* See Notice to Authors No. 7 in *J.C.S. Perkin II*, 1975, Index issue.

angles appear to imply that this ring adopts an envelope form in all three compounds, evaluation of the deviations indicates that ring A approximates to an envelope form in compounds (1) and (5), whereas the corresponding rings in (5') and (6) are more intermediate in nature. In none of these examples, however, is the ring very close to an ideal half-chair form as that conformation would have a greater number of more nearly eclipsed C=O to C-H interactions than occur in any of the forms actually found. In addition to these small differences in the (5) and (5') ring A shapes, a highly significant finding is that the C(2) displacement is to the β -side in (5) whereas it is

to the α -side in (5'). Inspection of Dreiding molecular models shows that a C(2) β -side displacement produces more severe overcrowding of the 1β - and 11α -hydrogen



atoms than occurs with the C(2) α -side displacement. The differences between the C(1)-C(10)-C(9)-C(11) and C(5)-C(10)-C(9)-C(8) torsion angles [33.5 and -24.8° in

⁷ D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.

⁸ R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.

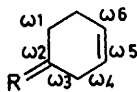
⁹ A. T. McPhail and R. W. Miller, *J.C.S. Perkin II*, 1975, 1180.

¹⁰ P. A. Luhan, Ph.D. Dissertation, Duke University, 1973.

(5); 40.9 and -16.3° in (5')] indicate that the short $H(1\beta) \cdots H(11\alpha)$ interaction is relieved to some extent in (5) by a mean clockwise rotation of 8° about the C(9)-C(10) bond from the conformation found in (5') with concomitant change in the ring B conformation

TABLE 5

Endocyclic torsion angles ($^\circ$) in some selected steroid rings



(a) β,γ -Cyclohexenone A rings, R = O

	(1) ^a	(5) ^b	(5') ^b	(6) ^c
ω_1	47.6	-44.7	49.2	-46
ω_2	-47.5	44.3	-55.4	55
ω_3	20.6	-20.6	31.6	-35
ω_4	7.1	-3.9	-1.7	7
ω_5	-5.6	2.2	-2.9	0
ω_6	-22.4	22.6	-21.4	20
$\Delta(C_2 - HC)$ ^e	62.1	52.8	40.2	24
$\Delta(C_s - E)$ ^f	14.6	8.5	21.0	31

(b) Cyclohexene B rings, R = H, H

	(1) ^a	(5) ^b	(5') ^b	(7) ^d
ω_1	47.7	51.2	46.5	49
ω_2	-62.5	-59.1	-63.1	-61
ω_3	43.4	39.0	47.7	43
ω_4	-11.2	-12.0	-17.8	-15
ω_5	-3.1	4.9	2.0	3
ω_6	-15.5	-24.8	-16.3	-20
$\Delta(C_2 - HC)$ ^e	11.7	29.9	4.7	14
$\Delta(C_s - E)$ ^f	57.0	39.0	67.8	53

^a Calc. from the co-ordinates provided in ref. 1 which lists those for the mirror image of the natural series. ^b Present work. ^c Ref. 9. ^d Ref. 10. ^e $\Delta(C_2 - HC) = |\omega_5| + |\omega_4 - \omega_6| + |\omega_1 - \omega_3|$. ^f $\Delta(C_s - E) = |\omega_4| + |\omega_5| + |\omega_3 + \omega_6| + |\omega_1 + \omega_2|$.

from the approximately ideal half-chair form in (5') to a higher-energy intermediate form in (5).¹¹ The co-occurrence of molecules possessing these two different conformations in the same crystal is clearly a consequence of crystal packing forces, especially hydrogen bonding. The carbonyl oxygen atoms of (5) molecules participate in hydrogen bonds to the hydroxy-groups of

¹¹ See e.g., R. Bucourt, *Topics Stereochem.*, 1974, **8**, 159, and references therein.

¹² C. Altona, H. J. Geise, and C. Romers, *Tetrahedron*, 1968, **24**, 13.

adjacent (5) molecules whereas the carbonyl oxygen atom of (5') molecules is subjected only to weak van der Waals type forces in the crystal (*vide supra*). From these observations and the results of earlier structural studies we conclude that the low-energy form of ring A in 3-oxo- $\Delta^{5,10}$ -steroids approximates more closely to a C(2) α -side envelope conformation than to a half-chair form. However, the corresponding higher energy form in which C(2) is displaced to the β -side is capable of coexistence to an appreciable extent in the appropriate environment and may have a significant population in biological systems and in solution.

The c rings in (5) and (5') molecules adopt the usual chair conformations which differ significantly only in the torsion angle around the C(8)-C(9) bond [-56.5 in (5), -60.0° in (5')] as a consequence of the different ring B conformations already described.

Deviations of the endocyclic torsion angles in the D rings of (5) and (5') from ideal C(13)-envelope [$\Delta(C_s - E) = |\omega_{15,16}| + |\omega_{14,15} + \omega_{16,17}| + |\omega_{13,14} + \omega_{13,17}|$] and C(16)-half-chair [$\Delta(C_2 - HC) = |\omega_{13,17} - \omega_{14,15}| + |\omega_{15,16} - \omega_{16,17}|$] symmetry-constrained values [$\Delta(C_s - E)$ 12.0 in (5), 22.6 in (5'); $\Delta(C_2 - HC)$ 35.4 in (5), 23.6° in (5')] indicate that the ring has an intermediate form in (5') but lies closer to a C(13)-envelope form in (5). An alternative description¹² of these conformations may be made in terms of the maximum torsion angle ϕ_m [48.8 in (5), 46.8° in (5')] and phase angle of pseudorotation Δ [27.3 in (5), 18.8° in (5')]. The conformations found here are quite typical for ring D in steroids bearing 17 β -hydroxy groups^{13,14} and their different forms reflect variations in crystal packing forces.

We thank the U.S. National Science Foundation for funds towards the purchase of the diffractometer and partial financial support (P. A. L. and P. S. W. T.) through a Science Development grant to Duke University. Calculations were performed on an IBM 370/165 computer located at the Triangle Universities Computation Centre and supported by a grant of computer time from Duke University.

[6/761 Received, 21st April, 1976]

¹³ C. Romers, C. Altona, H. J. C. Jacobs, and R. A. G. DeGraff, in 'Terpenoids and Steroids,' ed. K. H. Overton, Chem. Soc. Specialist Periodical Reports, vol. 4, 1973.

¹⁴ G. A. Sim, in 'Molecular Structure by Diffraction Methods,' eds. G. A. Sim and L. E. Sutton, Chem. Soc. Specialist Periodical Report, vol. 2, 1974; vol. 3, 1975.