obligatory initial 1,5 bonding at the acetylenic termini. (d) Taken in part from the Dissertation submitted in partial fulfillment for the requirements of the Ph.D. degree of D. M. Chihal, University of New Orleans, 1975.

(2) (a) For a comprehensive review of the di-π-methane rearrangement see S. S. Hixson, P. S. Mariano, and H. E. Zimmerman, *Chem. Rev.*, **73**, 531 (1973). (b) For a classic early example of the di-π-methane reaction see H. E. Zimmerman and P. S. Mariano, *J. Am. Chem. Soc.*, **91**, 1718 (1969).

(3) B. Halton, M. Kulig, M. A. Battiste, J. Perreten, D. M. Gibson, and G. W. Griffin, *J. Am. Chem. Soc.*, **93**, 2327 (1971).

(4) (a) Presented in part at the 28th Southwest Regional Meeting of the American Chemical Society, Baton Rouge, La., Dec 6–8, 1972, Abstract No. 222, p 76. (b) D. C. Lankin, D. M. Chihal, G. W. Griffin, and N. S. Bhacca, *Tetrahedron Lett.*, 4009 (1973); D. C. Lankin, D. M. Chihal, N. S. Bhacca, and G. W. Griffin, *J. Am. Chem. Soc.*, **97**, 7133 (1975).

(5) H. Gilman, "Organic Syntheses", Collect. Vol. I, Wiley, New York, N.Y., 1961, p 77.

(6) *Caution:* It has been noted in one case that the alcohol **6** induces an allergic reaction upon contact even with the vapors with the response becoming increasingly severe upon repeated exposure. Symptoms include periorbital edema, erythema, and nausea.

(7) Irradiation of **7b** under the same conditions likewise gives a mixture of **7a** and **7b** of similar composition.

(8) K. Nakanishi, "Infrared Absorption Spectroscopy", Holden-Day, San Francisco, Calif., 1962, p 25.

(9) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2d ed, Pergamon Press, Oxford, 1969, p 301.

(10) F. A. Bovey, "Nuclear Magnetic Resonance Spectroscopy", Academic Press, New York, N.Y., 1969, p 251.

(11) The nomenclature for the acetylenic cyclopropanes **8**, **9**, **10**, and **11** is in accord with "IUPAC Tentative Rules for the Nomenclature of Organic Chemistry, Section E. Fundamental Stereochemistry, Rule E-3.3", *J. Org. Chem.*, **35**, 2849 (1970). The designations *r*, *c*, and *t* refer to the reference center and cis and trans substituents, respectively.

(12) (a) C. G. Hatchard and C. A. Parker, *Proc. R. Soc. London, Ser. A*, **235**, 518 (1956). (b) It has been shown experimentally, ref 12c, and theoretically, ref 12d, that irradiation of samples in cylindrical cells in a Merry-Go-Round apparatus may seriously affect the observed quantum yield when the sample cell contains a solvent of different refractive index from that employed in the actinometer cell and similar criticisms might be advanced concerning our determinations with **7a** and **7b** despite the fact that the Mini-Go-Round was employed with flat quartz cuvettes. In view of our ability to reproduce the reported quantum yield data for the photoisomerization of 1,1,3-triphenyl-3,3-dimethyl-1-propene, it appears that such arguments are invalid here, perhaps because of the nearly monochromatic light source used and the flat cell surfaces exposed. (c) G. F. Vesley, *Mol. Photochem.*, **3**, 193 (1971). (d) M. D. Shetlar, *ibid.*, **5**, 287 (1973).

(13) (a) A sample of this compound was generously supplied by Professor H. E. Zimmerman, Department of Chemistry, University of Wisconsin, Madison, Wis. (b) We wish to thank Professors Zimmerman and Hixson for communication of data regarding the compounds **12a** and **12b** prior to publication and for fruitful correspondence and discussions during the preparation of this manuscript.

(14) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2d ed, Pergamon Press, Oxford, 1969, p 286.

(15) The risks inherent in relying solely on physical methods for structure elucidation have been detailed recently [H. E. Zimmerman and L. M. Tolbert, *J. Am. Chem. Soc.*, **97**, 5497 (1975), ref 12]. We feel, however, that our cyclopropane stereochemical assignments are secure in view of the availability of all isomers, the reliability of NOE experiments, the validity of coupling constant data, and the total self-consistency of the interpretation in the case of these unstable, compounds which are otherwise difficultly accessible by alternate synthetic means.

(16) During the preparation of our initial publication (see Acknowledgment and p 542, ref 2a) the results of an independent investigation of the stereochemistry of the di-π-methane rearrangement at carbon atom 1 of a diene were reported. See H. E. Zimmerman, P. Baeckstrom, T. Johnson, and D. W. Kurtz, *J. Am. Chem. Soc.* **94**, 5504 (1972); **96**, 1459 (1974).

(17) (a) H. E. Zimmerman, R. W. Binkley, R. S. Givens, and M. A. Sherwin, *J. Am. Chem. Soc.*, **89**, 3932 (1967); (b) H. E. Zimmerman and A. C. Pratt, *ibid.*, **92**, 6259 (1970); **92**, 6267 (1970); (c) H. E. Zimmerman and A. A. Baum, *ibid.*, **93**, 3646 (1971); (d) H. E. Zimmerman, J. D. Robbins, R. D. McKelvey, C. J. Samuel, and L. R. Sousa, *ibid.*, **96**, 4630 (1974); **96**, 1974 (1974); (e) H. E. Zimmerman and G. E. Samuelson, *ibid.*, **89**, 5971 (1967); **91**, 5307 (1969).

(18) G. W. Griffin and N. R. Bertoniere in "Carbenes", Vol. 1, M. Jones, Jr., and R. A. Moss, Ed., Wiley, New York, N. Y., 1972, Chapter 3, p 311.

(19) D. S. Noyce and L. J. Dolby, *J. Org. Chem.*, **26**, 3619 (1961).

Formation of an Unusual Steroidal Oxetane and Its Transformation Products

Elliot L. Shapiro,* Lois Weber, Stuart Polovsky,[19] and James Morton

Natural Products Research Department, Schering Corporation, Bloomfield, New Jersey 07003

Andrew T. McPhail* and Kay D. Onan

Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706

Derek H. R. Barton

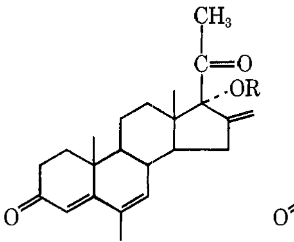
Chemistry Department, Imperial College, London SW 7 2AY, England

Received May 29, 1976

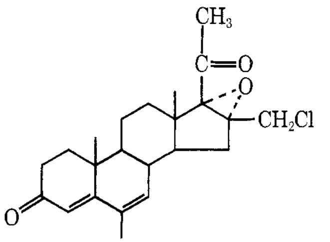
Chlorination of 6-chloro-16-methylene-17α-hydroxy-4,6-pregnadiene-3,20-dione (**1b**) gave unexpectedly 12% of an oxetane **3a**. Treatment of **3a** with base gave a D-homo seven-membered ring system **7** which with acid afforded the 15-acetyl androstadiene **9a**. The elucidation of these structures, and related transformations, are discussed, together with the application of single-crystal x-ray analyses for unequivocal structural determination.

In connection with studies of structural and pharmacological modifications of the progestogen, 6-chloro-16-methylene-17α-hydroxy-4,6-pregnadiene-3,20-dione acetate (**1a**),[1] two of us[2] sought to prepare 6-chloro-16β-chloromethyl-16α,17α-oxido-4,6-pregnadiene-3,20-dione (**2**).[3] Generation of the 16β-chloromethyl-16α,17α-oxido moiety from the 16-methylene-17-hydroxy unit has been accomplished previously by use of *N*-chlorosuccinimide[4] or chlorine.[3,5] With the 17-hydroxy **1b** available, it appeared that conversion to **2** might be effected, even though it was recognized that chlorination of the 4,6-dien-3-one system might also occur.[6] Using chlorine, the required compound **2** was obtained in moderate yield, but a significant amount of an unexpected oxetane, **3a**, was also produced. It is the formation of **3a**, its structural characterization, and subsequent transformation products (particularly **7** and **9**) which are the subject of this report. Elucidation of the constitution of **3a** was attempted initially by chemical transformations and interpretation of the various physical data presented in Tables I–III and Table X (elementary analyses, included in supplementary material), but this approach led to conflicting conclusions. Its structure, as well as structure **9a**, were finally established unequivocally by single-crystal x-ray analysis.

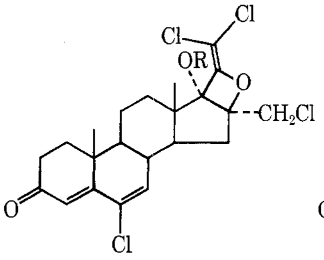
Treatment of **1b** with 1.1 equiv of chlorine (in the presence of 1.1 equiv of pyridine) for 5 min gave the 16β-chloromethyl 16α,17α-oxide (**2**) in 54% yield and another product in approximately 12% yield, as well as unreacted **1b**. Efforts to increase the yield of this minor product relative to the oxide **2**



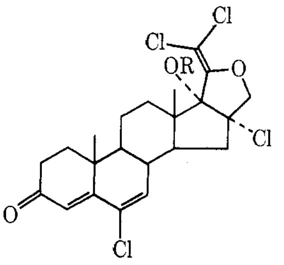
1a, $R = CH_3CO$
b, $R = H$



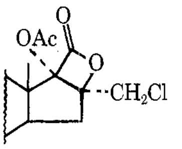
2



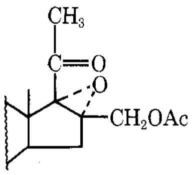
3a, $R = H$
b, $R = CH_3CO$



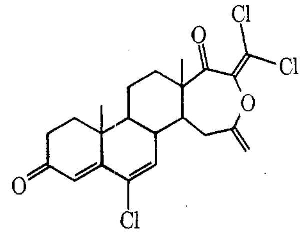
4a, $R = H$
b, $R = CH_3CO$



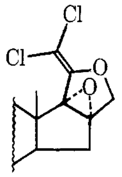
5



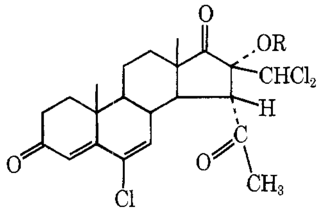
6



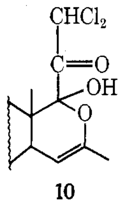
7



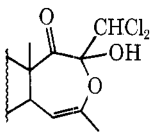
8



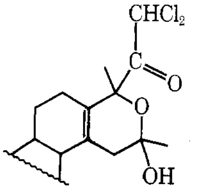
9a, $R = H$
b, $R = CH_3CO$



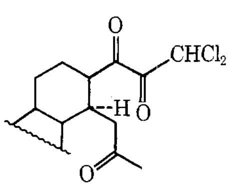
10



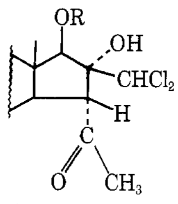
11



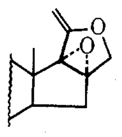
12



13



15a, $R = H$
b, $R = CH_3CO$



16

by varying medium and conditions proved fruitless. The analytical and spectral data revealed that this minor product possessed four chlorine atoms, a hydroxyl group, and the unchanged A/B ring system of **1b**, but lacked the 17-acetyl group. Of the structures accommodating these facts, the oxetane and tetrahydrofuran systems depicted in **3a** and **4a** seemed most reasonable.

Retention of the tertiary 17-hydroxyl function in the product was suggested by its conversion to the corresponding acetate with trifluoroacetic anhydride, acetic acid, and *p*-TSA,[7] but not with acetic anhydride in pyridine. However, its exposure to various acid media failed to provide further structural information. For example, treatment with either $HClO_4$ (at room temperature or at 60 °C) or acetic acid gave no reaction, whereas with HCl in acetic acid or with zinc in ethanol complex mixtures resulted; neither of these mixtures was investigated beyond TLC analysis.

It appeared that cleavage of the dichloromethylene moiety at C-20 by ozonolysis to produce the corresponding lactone would be instructive in the differentiation of **3** vis-à-vis **4**. However, while ozonolysis (EtOAc, pyridine, −60 °C) of the acetate gave in a single experiment a product which exhibited an ir band at 1852 cm^{-1} suggestive of the presence of a β-lactone as in **5**, this transformation proved to be irreproducible. Other attempts to distinguish between **3** and **4** by treatment with $Pb(OAc)_4$ were unsuccessful.

Consideration of structures **3** and **4** suggested that it should be possible to differentiate chemically between their respective primary and tertiary 16α-chloro substituents. In a model experiment, the primary chloride of **2** was converted to the primary acetate **6** with KOAc in DMF at 80 °C; by analogy, **3b** would be expected to yield the corresponding acetate. In contrast, however, **3b** afforded starting material as the only recognizable product. Failure to effect this transformation suggested structure **4b** rather than **3b**, in contrast to the results of the ozonolysis experiment.

Further support for structure **3a** came from physical data for a compound which was obtained from **3a** in 80% yield by use of KOAc in refluxing acetone and in 90% yield from the acetate derivative (**3b**) by use of NaOH in methanol at room temperature. These data showed that the reactions had proceeded with retention of the dichloromethylene unit, loss of a chlorine atom, and generation of a possible methylene system. In addition, an increased intensity in the absorption band at 283 nm was noted. While these data are more compatible with structure **7** (derivable from **3**) than with structure **8** (derivable from **4**), definitive assignment was still precluded by lack of convincing evidence. This uncertainty was intensified by analysis of the data obtained for another compound (Tables I–III, **9a**) generated in approximately 45% yield from proposed **7** (or **8**) with $HClO_4$ in THF at 60 °C. A most significant feature of **9a** was that it contained a methyl group having an anomalous chemical shift of 2.72 ppm. Esterification with acetic anhydride in pyridine for 48 h at room temperature gave approximately 65% yield of an acetate derivative in which the corresponding methyl signal appeared at 2.64 ppm. Possible structures which were considered, i.e., **10–12** (with **13** as the common precursor) did not accommodate the data for **9a** or its acetate. Subsequent reduction of **9a** with $NaBH_4$ at 5 °C gave a crude substance (**14**) in 80% yield. Allylic oxidation of the 3-hydroxy group with MnO_2 then produced a compound (Tables I–III, **15a**) which NMR revealed to contain a secondary hydroxyl group and a methyl group with a signal at 2.36 ppm which shifted downfield to 2.54 ppm upon esterification of **15a** with acetic anhydride in pyridine.

In order to resolve these structural ambiguities and thereby allow the sequence of transformations to be rationalized, **3a** and **9a** were subjected to single-crystal x-ray analyses. Both structures were solved by direct noncentrosymmetric phase-

Table I. Analytical Data

Registry no.	Compd	Mp, °C^a	$[\alpha]_D^b$	Ir, cm$^{-1\,d}$	Mol wt	m/e^e
24431-77-4	**1b**	170–172 (sint 168)	−42	3448, 1718, 1653, 1600, 1585, 917, 909, 901	374.90	374
33146-09-7	**2**	137–139 (sint 135)	+57	1709, 1661, 1603, 1587, 1109, 877	409.34	408
60295-32-1	**3a**	275 dec	−1^c	3448, 1770 (vw), 1698 (vw), 1650, 1610, 1587, 1412	478.24	476
60295-33-2	**3b**	227–230	+21 +11^c	1757, 1672, 1618, 1595	520.28	518
60295-34-3	**5**			1852, 1761, 1669, 1618, 1600, 1235–1230	453.36	
60295-35-4	**6**	96–98 (sint 89)	+52.3	1754, 1718, 1667	432.93	
60295-36-5	**7**	216–218 (sint 214)	+24 +55^c	1701, 1667, 1610, 1587, 1427, 1414, 1247, 1225, 990; ($CHCl_3$) 1701 (w), 1664, 1610, 1592	441.77	440
60295-37-6	**8**	200 dec (sint 160)		1664, 1613, 1595, 1053, 1043	441.80	440
60295-38-7	**9a**	232 dec (sint 228)	+107 +150^c	3344, 3300, 1751, 1686, 1653, 1597, 1580	459.79	458
60295-39-8	**9b**	263 dec	+129^c	1779, 1764, 1761, 1675, 1618, 1597	501.83	
60305-59-1	**15a**	222 dec		3390, 1695, 1669, 1610, 1587	461.81	460
60295-04-7	**15b**			3268, 3172, 1754, 1701, 1668, 1621, 1197, 1232, 1073	503.84	502
60295-05-8	**16**	205–211 (sint 180)	+107	1681, 1664, 1639 (sh), 1610, 1787, 1410, 1025, 1010, 891.3	372.88	

^{a} Kofler hot-stage microscope or capillary melting point apparatus and are uncorrected. ^{b} Dioxane, unless otherwise indicated, at 25 °C at about 1% concentration. ^{c} Pyridine. ^{d} Nujol. ^{e} Varian MAT CH5 spectrometer using electron impact source at 70 eV and at 2.5 °C.

Table II. Analytical Data—Ultraviolet Absorption

Compd	λ_{max}	$\epsilon^{a,b}$	λ_{max}	$\epsilon^{c,f}$
1b	285	22 200		
2	283	21 400	278	22 100
			208^d	4 400
3a	283	22 700^c	278	23 700
	207.5	16 000^c	208	15 100
3b	282.5	22 980^c	278	23 500
	209	14 800^c	208	14 700
5	282	17 400		
6	282	21 700		
7	283	25 800		
8	283	20 800^c	278	21 200
	223	14 300^c	223	13 800
			207^e	10 100
9a	283	23 000		
9b	282	17 750		
15a	284	22 400		
15b	283	17 000		
16	283	20 400^c	283	22 100
	206.5	13 700^c	206.5	13 700

^{a} MeOH as solvent. ^{b} Unless otherwise indicated, Cary 11 spectrometer. ^{c} Cary 118CX spectrometer. ^{d} Point on rising slope to 190 nm. ^{e} Inflection. ^{f} CH_3CN as solvent.

determining procedures and the nonhydrogen atom positional and thermal parameters were refined by full-matrix least-squares 1 and 2. Final positional and thermal parameters for the carbon, chlorine, and oxygen atoms (Tables V and VI) and calculated positions for the hydrogen atoms (Tables VII and VIII) are included in the supplementary material.[8]

Corresponding interatomic distances and valency angles, presented in Table IV, all agree well for chemically equivalent bonds and lie close to accepted values except in the oxetane ring of **3a** and ring D of **9a**. The strain involved in the oxetane ring of **3a** results in elongated C(16)–O(25) [1.54 (2) Å] and C(16)–C(17) [1.59 (2) Å] bonds. In **9a** bonds C(15)–C(16) [1.584 (11) Å] and C(16)–C(17) [1.574 (11) Å] are longer than normal owing to the highly substituted nature of ring D.

Complete lists of torsion angles defining the molecular conformations are in Table IX.[8] In **3a**, ring A with $\Delta(C_2)$ = 31°, $\Delta(C_s)$ = 25°,[9] and ring B with $\Delta(C_2)$ = 25°, $\Delta(C_s)$ = 25°, are intermediate between half-chair and envelope[10] conformations. In **9a**, ring A approximates to a C(1)α envelope form [$\Delta(C_2)$ = 51°, $\Delta(C_s)$ = 4°] while ring B has a conformation which lies closer to a C(9)α–C(10)β half-chair form [$\Delta(C_2)$ = 26°, $\Delta(C_s)$ = 40°]. In both compounds ring C has a distorted chair conformation, and ring D adopts a form intermediate between a C(14) envelope (C_s) and a C(16) half-chair (C_2) form characterized[11] by ϕ_{max} = 49°, $\Delta = -22°$ in **3a**, and ϕ_{max} = 48°, $\Delta = -56°$ in **9a**. The oxetane ring of **3a** has endocyclic torsion angles of ±9° and accordingly deviates by a small amount from planarity, the displacement of C(20) being to the α side of the C(17),C(16),O(25) plane in order to minimize nonbonded interactions with the C(13)-methyl group.

In the solid state molecules of **3a** and **9a** are linked by O–H···O hydrogen bonds between the tertiary hydroxyl group and the carbonyl oxygen of ring A. For **3a** the association occurs between molecules related by unit translations along both the *b* and *c* directions with O(24)···O(23′) = 3.12 Å,[12] and a C(17)–O(24)···O(23′) angle of 98°. In crystals of **9a** the molecules are associated by hydrogen bonding around the 2_1 screw axis along the *c* direction with O(25)···O(23″) = 2.97 Å,[12] and a C(16)–O(25)···O(23″) angle of 124°. All other short intermolecular separations are of the van der Waals type.

With the structures of **3a** and **9a** firmly established by the

Table III. ^{1}H NMR Data[a]

Compd	
1b	0.86 (13-CH$_3$), 1.18 (10-CH$_3$), 2.34 (20-CH$_3$), 5.10, 5.30 (16-CH$_2$), 6.31 (4-H), 6.31 (7-H), 3.28 (17-OH)
2	1.12 (13-CH$_3$), 1.17 (10-CH$_3$), 2.26 (20-CH$_3$), 6.33 (4-H), 6.26 (d, J = 2.2 Hz) (7-H), 3.68, 3.76 (ab doublets, J = 12.5 Hz) (16-CH$_2$Cl)
3a	0.99 (13-CH$_3$), 1.04 (10-CH$_3$), 6.05 (4-H), 6.44 (d, J = 2 Hz) (7-H), 6.57 (17-OH), 3.91, 4.06 (ab doublets, J = 12.5 Hz with D$_2$O sharpened) (16-CH$_2$Cl)
3b	1.19 (13-CH$_3$), 1.26 (10-CH$_3$), 2.16 (17-OCOCH$_3$), 6.35 (4-H), 6.26 (d, J = 1.5 Hz) (7-H), 3.98, 4.06 (ab doublets, J = 11.8 Hz) (16-CH$_2$Cl)
6	1.09 and 1.13 (10-CH$_3$ and 13-CH$_3$), 2.09 (16-CH$_2$O-C(=O)CH$_3$), 2.26 (20-CH$_3$), 4.21 and 4.50 (J = 12 Hz) (16-CH$_2$OAc), 6.25 (J = 2 Hz) (7-H), 6.33 (4-H)
7	1.17 (13-CH$_3$), 1.26 (10-CH$_3$) 6.37 (4-H), 6.47 (broad) (7-H), 5.04 and 4.90 (2 triplets, J = 1.8 Hz) (16-CH$_2$)
8	1.08 (13-CH$_3$), 1.13 (10-CH$_3$), 4.09 and 4.34 (ab doublets, 10.5 Hz) (16-CH$_2$), 6.15 (d, J = 2 Hz) (7-H), 6.29 (4-H)
9a	1.18 (13-CH$_3$, and 10-CH$_3$), 6.44 (4-H), 5.93 (d, J = 2 Hz) (7-H), 5.98 (16-CHCl$_2$), 5.34 (16-OH) (disappears with D$_2$O), 3.82 (d, 12 Hz) (15-H), 2.72 (15-COCH$_3$)
9b	1.15 and 1.18 (10-CH$_3$ and 13-CH$_3$), 6.30 (4-H), 5.89 (broad) (7-H), 5.93 (16-CHCl$_2$), 3.84 (d, 12 Hz) (slightly broadened, J = 12 Hz) (15-H), 2.64 (15-COCH$_3$)
15a	0.87 (13-CH$_3$), 1.09 (10-CH$_3$), 6.01 (4-H), 5.93 (d, J = 2.0 Hz) (7-H), 3.35 (d, J = 12 Hz) (15-H), 3.67 (d, J = 5.5) (singlet with D$_2$O) (17-H), 6.07 (16-CHCl$_2$), 2.36 (15-COCH$_3$), 5.20 (d, J = 5.5) (17-OH), 5.60 (16-OH) (disappears with D$_2$O)
15b	1.02 (13-CH$_3$), 1.15 (10-CH$_3$), 2.12 (17-OCOCH$_3$), 2.54 (15-COCH$_3$), 3.34 and 3.54 (15-H), 4.96 (17-H), 4.64 (16-OH), 5.82 (16-CHCl$_2$), 5.85 (d, J = 2 Hz) (7-H), 6.30 (4-H)
16	1.09 (13-CH$_3$), 1.16 (10-CH$_3$), 4.20 and 4.54 (ab doublets, J = 1.8 Hz) (20 = CH$_2$), 3.97 and 4.21 (ab doublets, 10.5 Hz) (16-CH$_2$), 6.20 (d, J = 2.2 Hz) (7-H), 6.32 (4-H)

[a] Varian A-60A spectrometer and CDCl$_3$ (unless otherwise stated), with chemical shifts given in parts per million downfield from Me$_4$Si (δ). [b] Me$_2$SO-d_6. [c] NMR taken on crude product.

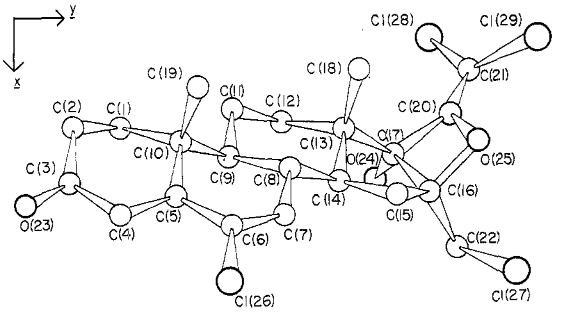


Figure 1. Atom numbering scheme and conformation of **3a**.

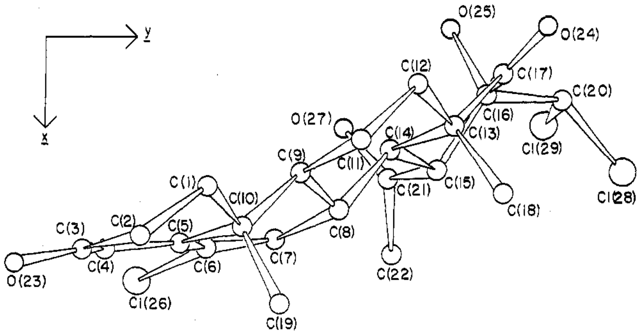
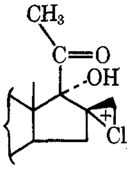


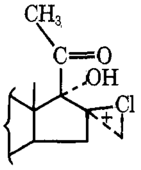
Figure 2. Atom numbering scheme and conformation of **9a**.

x-ray analyses, the sequence of transformations may be rationalized in the following manner.

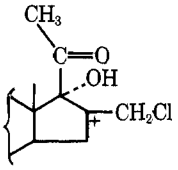
Chlorination of **1b** may afford an α- or β-chloronium species such as depicted in **17** or **18**. Attack by the 17α-hydroxyl group at the incipient C(16) carbonium species of **18** would readily produce oxide **2**. Transformation of **17** to **2** would appear less likely to occur except through the formation of a species which approaches canonical form **19**. However, polarization of the C(20) carbonyl bond with subsequent attack at C(16) as shown in **20** would lead to **21**.



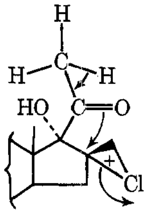
17



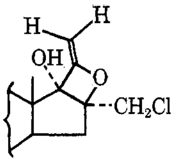
18



19



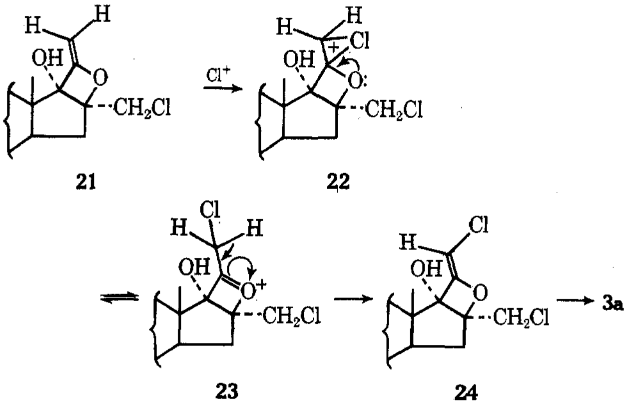
20



21

Chlorination of the C(20) methylene group may be visualized as proceeding in a stepwise manner involving electron donation by the oxetane oxygen as shown in the sequence **21** → **22** → **23** → **24** (Scheme I), with repetition of this process to yield 21,21-dichloro **3a**. (Reference 13 includes a less preferred process.)

Scheme I



23 **24**

Transformation of **3** to **7** may be visualized as proceeding

Table IV. Interatomic Distances (Å) and Valency Angles (deg), with Estimated Standard Deviations in Parentheses

A. Bond Lengths

	3a	**9a**		**3a**	**9a**
C(1)–C(2)	1.51 (3)	1.540 (15)	C(13)–C(18)	1.54 (2)	1.553 (12)
C(1)–C(10)	1.54 (2)	1.590 (13)	C(14)–C(15)	1.52 (2)	1.563 (11)
C(2)–C(3)	1.50 (2)	1.469 (15)	C(15)–C(16)	1.55 (2)	1.584 (11)
C(3)–C(4)	1.44 (3)	1.489 (17)	C(15)–C(21)		1.514 (12)
C(3)–O(23)	1.26 (2)	1.216 (11)	C(16)–C(17)	1.59 (2)	1.574 (13)
C(4)–C(5)	1.37 (2)	1.355 (13)	C(16)–C(20)		1.511 (13)
C(5)–C(6)	1.45 (2)	1.466 (12)	C(16)–C(22)	1.51 (2)	
C(5)–C(10)	1.53 (2)	1.501 (13)	C(16)–O(25)	1.54 (2)	1.405 (10)
C(6)–C(7)	1.33 (2)	1.307 (12)	C(17)–C(20)	1.52 (2)	
C(6)–Cl(26)	1.76 (2)	1.767 (8)	C(17)–O(24)	1.38 (2)	1.200 (11)
C(7)–C(8)	1.52 (2)	1.523 (12)	C(20)–C(21)	1.29 (2)	
C(8)–C(9)	1.57 (2)	1.552 (12)	C(20)–O(25)	1.40 (2)	
C(8)–C(14)	1.53 (2)	1.511 (10)	C(20)–Cl(28)		1.767 (10)
C(9)–C(10)	1.57 (2)	1.541 (12)	C(20)–Cl(29)		1.778 (11)
C(9)–C(11)	1.52 (2)	1.561 (12)	C(21)–C(22)		1.432 (12)
C(10)–C(19)	1.57 (2)	1.526 (11)	C(21)–O(27)		1.247 (11)
C(11)–C(12)	1.54 (2)	1.552 (13)	C(21)–Cl(28)	1.69 (2)	
C(12)–C(13)	1.54 (2)	1.512 (12)	C(21)–Cl(29)	1.75 (2)	
C(13)–C(14)	1.54 (2)	1.540 (11)	C(22)–Cl(27)	1.83 (2)	
C(13)–C(17)	1.57 (2)	1.511 (12)			

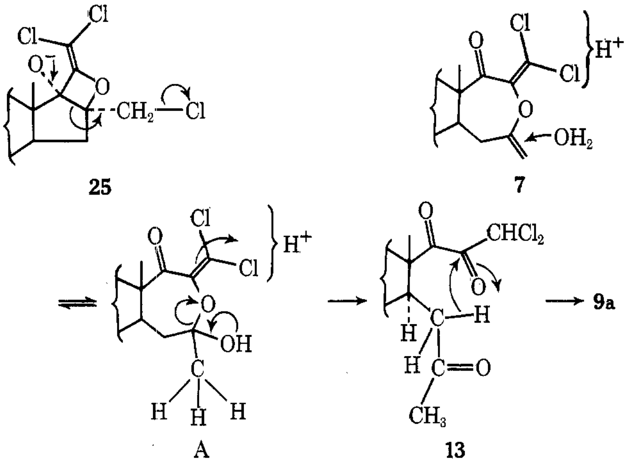
B. Valency Angles

	3a	**9a**		**3a**	**9a**
C(2)–C(1)–C(10)	111.8 (15)	109.9 (8)	C(8)–C(14)–C(15)	117.4 (14)	121.6 (6)
C(1)–C(2)–C(3)	112.0 (14)	113.3 (9)	C(13)–C(14)–C(15)	105.2 (12)	103.8 (6)
C(2)–C(3)–C(4)	118.3 (15)	118.8 (8)	C(14)–C(15)–C(16)	99.8 (13)	99.4 (6)
C(2)–C(3)–O(23)	122.3 (15)	122.8 (11)	C(14)–C(15)–C(21)		115.4 (6)
C(4)–C(3)–O(23)	119.1 (16)	118.3 (10)	C(16)–C(15)–C(21)		113.8 (6)
C(3)–C(4)–C(5)	122.5 (9)	120.8 (9)	C(15)–C(16)–C(17)	109.1 (12)	103.6 (7)
C(4)–C(5)–C(6)	123.6 (15)	121.7 (9)	C(15)–C(16)–C(20)		115.7 (7)
C(4)–C(5)–C(10)	121.3 (14)	123.7 (9)	C(15)–C(16)–C(22)	119.8 (13)	
C(6)–C(5)–C(10)	115.1 (13)	114.5 (7)	C(15)–C(16)–O(25)	113.3 (12)	113.9 (6)
C(5)–C(6)–C(7)	126.8 (15)	125.5 (8)	C(17)–C(16)–C(20		111.8 (7)
C(5)–C(6)–Cl(26)	116.2 (12)	116.8 (6)	C(17)–C(16)–C(22)	114.4 (13)	
C(7)–C(6)–Cl(26)	117.0 (12)	117.5 (6)	C(17)–C(16)–O(25)	87.3 (10)	104.8 (7)
C(6)–C(7)–C(8)	119.9 (13)	122.9 (7)	C(20)–C(16)–O(25)		106.6 (7)
C(7)–C(8)–C(9)	111.2 (11)	107.5 (7)	C(22)–C(16)–O(25)	108.5 (11)	
C(7)–C(8)–C(14)	114.8 (7)	115.6 (7)	C(13)–C(17)–C(16)	102.3 (12)	108.7 (7)
C(9)–C(8)–C(14)	109.9 (13)	108.8 (6)	C(13)–C(17)–C(20)	116.4 (11)	
C(8)–C(9)–C(10)	109.4 (12)	112.0 (6)	C(13)–C(17)–O(24)	112.9 (11)	128.9 (9)
C(8)–C(9)–C(11)	112.6 (11)	112.7 (7)	C(16)–C(17)–C(20)	85.0 (10)	
C(10)–C(9)–C(11)	114.7 (11)	113.8 (7)	C(16)–C(17)–O(24)	119.8 (11)	122.4 (8)
C(1)–C(10)–C(5)	110.8 (12)	109.7 (7)	C(20)–C(17)–O(24)	117.1 (13)	
C(1)–C(10)–C(9)	109.5 (14)	109.8 (7)	C(16)–C(20)–Cl(28)		113.3 (7)
C(1)–C(10)–C(19)	109.9 (12)	109.0 (7)	C(16)–C(20)–Cl(29)		112.1 (7)
C(5)–C(10)–C(9)	108.3 (11)	108.6 (7)	C(17)–C(20)–C(21)	138.1 (15)	
C(5)–C(10)–C(19)	106.4 (13)	108.5 (6)	C(17)–C(20)–O(25)	95.2 (11)	
C(9)–C(10)–C(19)	111.8 (11)	111.1 (7)	C(21)–C(20)–O(25)	126.6 (14)	
C(9)–C(11)–C(12)	112.3 (12)	112.6 (7)	Cl(28)–C(20)–Cl(29)		109.0 (5)
C(11)–C(12)–C(13)	112.2 (14)	110.3 (7)	C(15)–C(21)–C(22)		117.9 (7)
C(12)–C(13)–C(14)	106.7 (12)	111.0 (7)	C(15)–C(21)–O(27)		119.1 (8)
C(12)–C(13)–C(17)	115.3 (14)	114.6 (7)	C(20)–C(21)–Cl(28)	123.0 (13)	
C(12)–C(13)–C(18)	109.6 (12)	109.4 (7)	C(20)–C(21)–Cl(29)	121.4 (13)	
C(14)–C(13)–C(17)	101.1 (11)	102.3 (7)	C(22)–C(21)–O(27)		123.0 (8)
C(14)–C(13)–C(18)	112.9 (14)	113.4 (6)	Cl(28)–C(21)–Cl(29)	115.6 (9)	
C(17)–C(13)–C(18)	110.9 (12)	106.0 (7)	C(16)–C(22)–Cl(27)	108.7 (11)	
C(8)–C(14)–C(13)	112.0 (11)	111.3 (6)	C(16)–O(25)–C(20)	91.3 (10)	

from the base generated anion **25** as depicted via ketonization of the 17α-hydroxyl group. The coupling exhibited in the NMR is consistent with the presence of an exocyclic methylene group. The increase in intensity of the band at 283 nm may be attributed to the chromophoric contribution of the conjugated unit contained in ring D of **7**.

Formation of **9a** may be considered to occur by the acid-catalyzed hydration of **7** followed by cleavage of species "A" to **13** and then recyclization to **9a** (Scheme II). The chemical shift of 2.72 ppm for the 15-acetyl methyl in **9a** is significantly further downfield than is usually found for methyl ketones (2.00–2.20 ppm) and merits some comment. Since the corresponding signal in acetate **9b** occurs at 2.64 ppm it does not appear likely that the deshielding effect is due to intramo-

Scheme II



lecular hydrogen bonding involving the hydroxyl group of **9a**. Although it is not revealed in the crystalline rotamer as shown by x-ray analysis (Figure 2), Dreiding model orientation of the 15-acetyl group indicates that in solution this grouping may lie close to the chlorine atoms of the 16β-dichloromethyl group, a feature reflected in solution NMR as a deshielding effect. A like conclusion would apply to **15a** and **15b** in which the ring D conformations would differ slightly from those in **9a** and **9b** owing to the absence of the 17-keto group. A substantial shielding effect would be expected from the spatial orientation of the 15-acetyl carbonyl relative to the 7 hydrogen and this is indeed observed in the chemical shifts for this proton in **9a, 9b, 15a,** and **15b,** all of which display signals more upfield than those in **1, 2, 3a, 3b, 6,** and **7.**

The presence of a singlet absorption at 2.36 ppm in **15a** indicates that mild $NaBH_4$ reduction (vide supra) of **9a** occurred selectively at the 17 carbonyl in preference to the 15 carbonyl. Reduction to form a 15(1′-hydroxyethyl) unit in this reaction would have been indicated by coupling of the terminal methyl group with the hydrogen geminal to the hydroxy group.

The 17-hydroxy group in **15a** is probably β oriented since approach of the reducing agent from the β side of **9a** would be severely hindered by the combined steric effects of the 16β-dichloromethyl and 13-methyl groups and would thus be more likely to occur from the α side which has the less bulky 16α-hydroxy group.

Finally, we note (Table II) the lower wavelength ultraviolet absorptions for compounds **3a** and **3b,** as well as **8** and **16,** which are attributable to the exocyclic methylene unit. The dichloromethylene moiety exocyclic to the four-membered ring system in **3a** and **3b** has its maximum at 208 nm. The exocyclic dichloromethylene grouping of the five-membered ring system in **8**, however, has an ultraviolet maximum at 223 nm, with an inflexion at 207 nm, whereas the related methylene (hydrogens attached to the 20 carbon) has its lower wavelength absorption at 206.5 nm. The effect of the allylic 16,17-oxide unit on the lower wavelength absorption of the methylene group in **8** and **16** has not been defined.

Experimental Section

Crystal Data. $C_{22}H_{24}Cl_4O_3$ (**3a**), mol wt 478.3. Orthorhombic, $a = 26.95$ (3), $b = 10.83$ (2), $c = 7.44$ (2) Å, $U = 2172$ Å^3, d_m (flotation) = 1.45 g cm^{-3}, $Z = 4$, $d_c = 1.463$ g cm^{-3}, $F(000) = 992$. Cu Kα radiation, $\lambda = 1.542$ Å; absorption coefficient for Cu Kα radiation, $\mu = 51.2$ cm^{-1}. Space group $P2_12_12_1(D_4{}^2)$ uniquely established from the systematic absences: $h00$ when $h \neq 2n$, $0k0$ when $k \neq 2n$, $00l$ when $l \neq 2n$.

$C_{22}H_{25}Cl_3O_4$ (**9a**), mol wt 459.8. Orthorhombic, $a = 13.09$ (1), $b = 17.69$ (1), $c = 9.47$ (1) Å, $U = 2193$ Å^3, d_m (flotation) = 1.39 g cm^{-3}, $Z = 4$, $d_c = 1.393$ g cm^{-3}, $F(000) = 960$. Mo Kα radiation, $\lambda = 0.7107$ Å; absorption coefficient for Mo Kα radiation, $\mu = 4.5$ cm^{-1}. Space group $P2_12_12_1(D_4{}^2)$ established by the systematic absences which were the same as for **3a.**

Crystallographic Measurements. Unit-cell dimensions for **3a** were obtained from rotation and zero-level Weissenberg photographs taken with Ni-filtered Cu Kα radiation. For **9a** preliminary unit-cell dimensions derived in a like manner were refined by least-squares treatment of the θ, χ, and ϕ angles for 40 reflections accurately centered on an Enraf-Nonius CAD 3 automated diffractometer (Zr-filtered Mo Kα radiation; 3° take-off angle).

Intensity data for the $hk0$-6 reciprocal lattice nets of **3a** were recorded photographically by the multiple-film equi-inclination Weissenberg method and estimated visually by comparison with a calibrated intensity strip. These data were assumed initially to be on a common scale as each level had been given approximately equal exposure times; absolute layer scales were derived at the end of the isotropic refinement cycles by correlation of $\Sigma|F_o|$ with $\Sigma|F_c|$. Application of spot-shape corrections and the usual Lorentz and polarization factors yielded 1402 independent structure amplitudes which were used in the structure analysis and refinement. No corrections were made for absorption or extinction.

For **9a** all unique intensity data up to 2θ 50° were measured on an Enraf-Nonius CAD 3 automated diffractometer (Zr-filtered Mo Kα radiation; 3° take-off angle) with a crystal of dimensions ca. 0.20 × 0.80 × 0.30 mm oriented so that the crystal b axis was parallel to the diffractometer ϕ axis. Data were recorded by the θ–2θ scanning technique with scan widths $(1.00 + 0.50 \tan \theta)$; stationary background measurements were made at each end of the scan range for a time equal to half the scan period. Instrument and crystal stability were monitored throughout by remeasuring the intensity of a strong standard reflection after each batch of 99 reflections; no significant variation was noted. From a total of 2222 measurements, 1243 reflections for which $I > 2.0\sigma(I)$, where $\sigma(I) = (\text{scan count} + \text{total background count})^{1/2}$, were used in the structure analysis and refinement. Absorption corrections determined from the ϕ dependence of the 0 8 0 reflection measured at $\chi = 90°$ were applied to these data which were then corrected for Lorentz and polarization effects.

Structure Analyses. The crystal structures were solved by direct noncentrosymmetric phase-determining procedures using MULTAN[14] with the 251 (**3a**) and 243 (**9a**) largest $|E|$ values. In each case the program was allowed to select four reflections in addition to the three origin defining reflections and the correct solutions corresponded to those sets with the highest figures-of-merit and lowest residuals.

For **3a** the initial structure model gave $R = 0.351$ when structure factors were calculated and this was reduced to 0.147 by full-matrix least-squares refinement of the atomic positional and isotropic thermal parameters. Inclusion of the hydrogen atoms at their calculated positions, with $B = 4.0$ Å^2, then decreased R to 0.141. After two more cycles of refinement during which the chlorine atoms were allowed to assume anisotropic thermal parameters, the anomalous scattering corrections for chlorine were introduced, and for structure factors calculated with coordinates corresponding to the known natural steroid absolute configuration R at 0.116 was significantly lower than for the mirror image ($R = 0.120$). Several further rounds of least-squares calculations during which the nonhydrogen atom parameters were varied brought the refinement to convergence at $R = 0.101$ when no parameter shift exceeded 0.10 times its estimated standard deviation. The analysis of **9a** followed a similar course from an initial R value of 0.286 to a final value of 0.059. Fractional atomic coordinates and thermal parameters for the nonhydrogen atoms (Tables V and VI) and calculated hydrogen atom coordinates (Tables VII and VIII) are included in the supplementary material. The lists of observed and calculated structure amplitudes (Tables XI and XII) are available upon request.[18]

Scattering factors used in all the structure-factor calculations were those for C, O, and Cl in the Cromer and Waber[15] compilation, with that for Cl corrected for anomalous dispersion;[16] for H the Stewart, Davidson, and Simpson[17] values were used. In the least-squares calculations $\Sigma w\Delta^2$ $(\Delta = |F_o| - |F_c|)$ was minimized, the weights w being assigned according to the scheme $\sqrt{w} = 1$ for $F_o < K$, and $\sqrt{w} = K/|F_o|$ for $|F_o| > K$ ($K = 25.0$ for **3a**, $= 15.0$ for **9a**).

Reaction of 16-Methylene-6-chloro-17α-hydroxy-4,6-pregnadiene-3,20-dione (1b) with Chlorine. Preparation of 6-Chloro-16β-chloromethyl-16α,17α-oxido-4,6-pregnadiene-3,20-dione (2) and 6,21,21-Trichloro-16α-chloromethyl-16β,20-oxido-17α-hydroxy-4,6,20-pregnatrien-3-one (3a). A solution containing 2.08 g of chlorine in CCl_4 (57.7 ml) was added to a solution of 10 g of **1b** contained in 500 ml of CH_2Cl_2 and 2.37 ml of pyridine. Consumption of chlorine occurred almost instantaneously. After approximately 7 min the solution was washed with water and evaporated to a residue which was chromatographed on 1100 g of silica gel eluting with ether–hexane (1:1 to 8.5:1.5) to obtain 2.3 g of unreacted **1b,** 5.9 g (54%) of **2**, crystallized from ether, and 1.5 g (11.5%) of the tetrachloro **3a**, crystallized from EtOAc.

Preparation of 6,21,21-Trichloro-16α-chloromethyl-16β,20-oxido-17α-hydroxy-4,6,20-pregnatrien-3-one 17-Acetate (3b). Trifluoroacetic anhydride (32 ml) was added dropwise in a 15-min time interval to a mixture consisting of 2.63 g of **3a,** 0.79 g of *p*-TsOH·H_2O, and 79 ml of AcOH with stirring, then stirring was maintained for 19 h. The reaction mixture was added to a 1-l. aqueous saturated sodium chloride solution. Insolubles were collected and dried (2.87 g) and then chromatographed on 287 g of silica gel, eluting with ether–hexane (2:3–3:2) to obtain after crystallization from EtOAc 2.14 g (75%) of **3b.**

Preparation of 6-Chloro-16-methylene-17-oxa-17a-dichloromethylenedi-D-homo-4,6-androstadiene-3,17b-dione (7). From 3a. A mixture consisting of 1.44 g of **3a,** 14.4 g of anhydrous KOAc, and 216 ml of acetone was refluxed for 2 h. The mixture was filtered, and the filtrate evaporated to dryness. The residue was taken up in CH_2Cl_2, washed with water, and evaporated to give a residue which was crystallized from EtOAc, 1.1 g (80%) of **7.**

From 3b. Exposure of 1.3 g of **3b** to 5 equiv of NaOH, in MeOH–CH_2Cl_2 for 15 min and workup gave **7** in approximately 90% conversion.

Preparation of 6-Chloro-15α-acetyl-16β-dichloromethyl-16α-hydroxy-4,6-androstadiene-3,17-dione (9a). A mixture consisting of 550 mg of **7,** 11 ml of H_2O, 5.5 ml of 70% $HClO_4$, and 38.5 ml of THF was heated at 60 °C for 29 h, then added to 10 volumes of water and extracted with CH_2Cl_2. Evaporation gave a residue of 585 mg which was chromatographed with 1000-μ silica gel plates, eluting with acetone–CH_2Cl_2, giving 430 mg (78%) of **9a,** crystallized from MeOH.

Preparation of 6-Chloro-15α-acetyl-16β-dichloromethyl-16α-hydroxy-4,6-androstadiene-3,17-dione 16-Acetate (5b). A solution consisting of 100 mg of **9a,** 2 ml of pyridine, and 1.0 ml of Ac_2O was kept at room temperature for 18 h. Usual workup gave a crude residue (98 mg). Crystallization from MeOH afforded 70 mg of 16-acetate **9b.**

6-Chloro-15α-acetyl-16β-dichloromethyl-16α,17β-dihydroxy-4,6-androstadien-3-one (15a). A. Reduction of 9a with $NaBH_4$. $NaBH_4$ (250 mg solid) was added to a solution of 0.5 g of **9a** in 5 ml of CH_2Cl_2, 5 ml of MeOH, and 1 ml of water, at 5 °C with stirring. After 25 min, dilute acetic acid was added to neutrality, most of the solvent was evaporated, water was added, and insolubles were collected. Crystallization from EtOAc gave 230 mg of **14** (uv showed no 3-keto-$\Delta^{4,6}$ absorption).

B. Generation of 15a with MnO_2. Activated MnO_2 (450 mg) was added to a solution of 150 mg of **14** in 15 ml of CH_2Cl_2, and the mixture stirred at room temperature for 1 h, then the insolubles were separated by filtration. Workup of the filtrate gave 120 mg (TLC, mainly one component), crystallized from EtOAc to yield 61 mg (41%) of **15a.**

6-Chloro-15α-acetyl-16β-dichloromethyl-16α,17β-dihydroxy-4,6-androstadien-3-one 17-Acetate (15b). The 17-hydroxy **15a** (20 mg) was added to 0.2 ml of Ac_2O and 0.4 ml of pyridine and maintained at room temperature for 61 h. The usual workup gave 21 mg of **15b** (TLC, approximately 5–10% impurity, visually).

Preparation of 6-Chloro-16α,17α:16a,20-dioxido-4,6,20-pregnatrien-3-one (16). *t*-BuOK (1.2 g) was added to a stirred solution consisting of 1.4 g of **2** and 118 ml of *t*-BuOH, under N_2, at room temperature. After 30 min, the mixture was added to 10 volumes of water and worked up in the usual way, giving 1.4 g of crude residue. Chromatography on 140 g of silica gel, eluting with mixtures of ether–hexane, gave, after crystallization from EtOAc, 0.48 g (37%) of **16.**

Preparation of 6-Chloro-21,21-dichloromethylene-16α,17α:16a,20-dioxido-4,6,20-pregnatrien-3-one (8). A 1.89-ml solution of chlorine (1.18 mmol) in CCl_4 was added to a solution consisting of 207 mg (0.555 mmol) of **16,** 100 mg of pyridine, and 11 ml of CH_2Cl_2, and the solution was stirred for 7 min. Although starch–iodide test paper was still positive, the solution was added to 10 ml of 0.1 N $Na_2S_2O_3$ solution and the mixture extracted with CH_2Cl_2. The residue from CH_2Cl_2 exhibited several components by TLC (silica gel). Separation of the components on 1000-μ silica gel preparative plate, developing with C_6H_{12}–EtOAc (4:1), then rechromatographing selected areas with $CHCl_3$ gave 23 mg of **8**, TLC indicating (H_2SO_4–MeOH stain) approximately 90–95% purity.

Reaction of 3b with Ozone. Attempted Preparation of 5. Ozone was added to a solution of 260 mg of **3b** in 16 ml of EtOAc and 5 ml of pyridine at −60 °C. Ten minutes after the development of blue solution, 6 ml of AcOH and 1 g of zinc dust were added and the solution was worked up in the usual way to afford a neutral fraction from which 14 mg (designated as **5**) was obtained after silica gel preparative plate [1000 μ, $CHCl_3$–EtOAc (9:1)] which still appeared by visual inspection of TLC to have 20–30% impurities.

Acknowledgments. We thank Dr. M. Yudis and Mrs. H. Marigliano for instructive NMR discussions.

Registry No.—14, 60295-06-9.

Supplementary Material Available. Tables of atomic coordinates and thermal parameters for the nonhydrogen atoms (Tables V and VI), hydrogen atom coordinates (Tables VII and VIII), torsion angles (Table IX), and elementary analyses (Table X) (10 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) E. L. Shapiro, L. Weber, H. Harris, C. Miskowicz, R. Neri, and H. L. Herzog, *J. Med. Chem.*, **15,** 716 (1972); (b) G. Teutsch, E. L. Shapiro, and H. L. Herzog, *ibid.*, **13,** 750 (1970); (c) E. L. Shapiro, L. Weber, G. Teutsch, H. Harris, R. Neri, and H. L. Herzog, *ibid.*, **16,** 649 (1973); (d) E. L. Shapiro, T. L. Popper, L. Weber, R. Neri, and H. L. Herzog, *ibid.*, **12,** 631 (1969); (e) G. Teutsch, L. Weber, G. Page, E. L. Shapiro, H. L. Herzog, R. Neri, and E. J. Collins, *ibid.*, **16,** 1370 (1973).

(2) E. L. Shapiro and L. Weber.

(3) R. W. Kierstead and P. Rosen, German Offen. 2 059 839 (June 16, 1971); *Chem. Abstr.*, **75,** 64118a (1971).

(4) (a) F. v. Werder, K. Bruckner, K.-H. Bork, H. Metz, B. Hampel, and H. J. Mannhardt, *Chem. Ber.*, **95,** 2110 (1962); the related 16β-bromomethyl-16,17-oxide moiety was obtained using *N*-bromosuccinimide, by R. D. Hoffsommer, D. Taub, and N. L. Wendler, *Chem. Ind.* (*London*), 251 (1961), and D. Taub, R. D. Hoffsommer, and N. L. Wendler, *J. Org. Chem.*, **29,** 3486 (1964).

(5) R. W. Kierstead and P. Rosen, U.S. Patents 3 655 653 (April 11, 1972) and 3 657 227 (April 18, 1972).

(6) R. W. Kierstead, J. Blount, K. E. Fahrenholtz, A. Faraone, R. A. LeMahieu, and P. Rosen, *J. Org. Chem.*, **35,** 4141 (1970); R. Wiechert, *Experientia*, **24,** 767 (1968).

(7) E. L. Shapiro, L. Finckenor, H. Pluchet, L. Weber, C. H. Robinson, E. P. Oliveto, H. L. Herzog, I. I. A. Tabachnick, and E. Collins, *Steroids*, **9,** 143 (1967).

(8) See paragraph at end of paper regarding supplementary material.

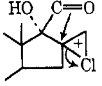
(9) Deviations from ideal half-chair (C_2) and envelope (C_s) conformations are expressed in terms of the endocyclic torsion angles, ω_{ij}, about the bonds between atoms C(*i*) and C(*j*). In ring A, $\Delta(C_2) = |\omega_{2,3} - \omega_{1,10}| + |\omega_{3,4} - \omega_{5,10}|$, $\Delta(C_s) = |\omega_{1,2} + \omega_{1,10}| + |\omega_{2,3} + \omega_{5,10}| + |\omega_{3,4} + \omega_{4,5}|$. In ring B, $\Delta(C_2) = |\omega_{5,10} - \omega_{8,9}| + |\omega_{5,6} - \omega_{7,8}|$, $\Delta(C_s) = |\omega_{8,9} + \omega_{9,10}| + |\omega_{5,10} + \omega_{7,8}| + |\omega_{5,6} + \omega_{6,7}|$.

(10) Also referred to in the literature as the sofa, 1,2-diplanar, and semiplanar form.

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

(12) O(23′) in **3a** requires transformation of the coordinates of Table V to x, $-1 + y$, $1 + z$; for O(23″) in **9a** the coordinates of Table VI should be transformed to $\frac{1}{2} - x$, $2 - y$, $\frac{1}{2} + z$.

(13) A less attractive process for the formation of **3a** would require mono- or dichlorination at C(21) to precede oxetane formation via a species such as B. However, supportive for our preferred sequence for **3a** formation



B

(although not proof) is the following. (a) When **2** was subjected to the same conditions as were employed for the **1a** → **3** transformation no reaction resulted. (b) Similar treatment of **1a** produced no 16,20-oxide **3b,** and **1a** was substantially recovered. (c) On the other hand, 21,21-dichloro **8** was obtained (9% yield) when **16** was treated similarly. [This furan system was first reported by D. Taub, R. D. Hoffsommer, and N. L. Wendler, *J. Org. Chem.*, **29,** 3486 (1964). In essence, we utilized their process for the preparation of **16** from **2.**] Although **16** contains a tetrahydrofuran system in contrast to the oxetane ring of **21,** it does not seem unreasonable to extend this transformation to the latter system.

(14) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27,** 368 (1971).

(15) D. T. Cromer and J. T. Waber, *Acta Crystallogr.*, **18,** 104 (1965).

(16) "International Tables for X-Ray Crystallography", Vol. III, Kynoch Press, Birmingham, England, 1967, pp 214–215.

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

(18) A. T. McPhail.

(19) Schering Postdoctoral Fellow, March 1974–Feb 1976.