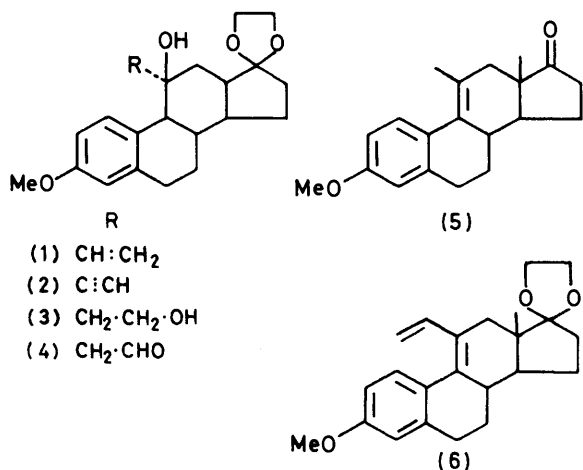


## Synthesis, Crystal and Molecular Structure of a 1,11-Etheno-steroid: 3-Methoxy-1,11-ethenoestra-1,3,5(10),9(11)-tetraen-17-one

By Colin G. Pitt,\* Douglas H. Rector, David H. White, and Mansukh C. Wani,\* Chemistry and Life Sciences Division, Research Triangle Institute, P.O. Box 12194, Research Triangle Park, North Carolina 27709, U.S.A. Andrew T. McPhail\* and Kay D. Onan, Paul M. Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706, U.S.A.

Methods of construction of a two carbon bridge between C(1) and C(11) of the steroid skeleton have been studied. Treatment of 17,17-ethylenedioxy-11 $\alpha$ -ethynyl-3-methoxyestra-1,3,5(10)-trien-11 $\beta$ -ol (2) with toluene-*p*-sulphonic acid in benzene gave a mixture of 3-methoxy-1' $\xi$ -methyl-1,11 $\xi$ -methanoestra-1,3,5(10),6,8,-pentaen-17-one (7) and the title compound (8). The latter was also obtained in poor yield from 17,17-ethylenedioxy-3-methoxy-11 $\alpha$ -(2-oxoethyl)estra-1,3,5(10)-trien-11 $\beta$ -ol (4) in hydrogen fluoride and in better yield (76%) from treatment of (2) with tris(triphenylsilyl) vanadate. Crystals of (8) are orthorhombic, space group  $P2_12_12_1$ ,  $a = 7.867(5)$ ,  $b = 30.036(20)$ ,  $c = 6.838(5)$  Å,  $Z = 4$ . The structure was solved by direct methods and refined by full-matrix least-squares calculations to  $R$  0.044 over 1 283 statistically significant reflections from diffractometer measurements. The modified steroid skeleton is very flat, the maximum deviation of any ring atom from the naphthalene plane being 0.635 Å. Ring B approximates to a C(7)  $\alpha$ -envelope form, ring C adopts a half-chair conformation, and ring D has a C(14)  $\alpha$ -envelope form.

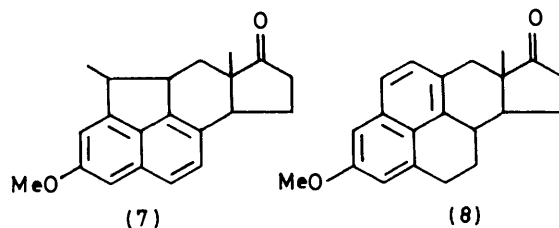
THE addition of bridges to the steroid skeleton represents a method of introducing substituents in positions which



ordinarily would be associated with gross conformational changes and a decreased affinity for the natural receptor proteins. Such is the case with a 1,11-methano- or -ethano-bridge, which serves to eliminate the severe non-bonded interactions which must exist in a 1- or 11 $\alpha$ -alkyl substituted estra-1,3,5(10)-triene. We have previously reported the synthesis and structure of several 1,11-methano-steroids.<sup>1</sup> Here we describe the extension of these studies to 1,11-etheno-steroids.

It has been shown<sup>1</sup> that treatment of 17,17-ethylenedioxy-3-methoxy-11 $\alpha$ -vinyl-1,3,5(10)-trien-11 $\beta$ -ol (1) with acids gives the 1' $\beta$ -methyl-1,11-methano-steroid (5). The reaction was presumed to proceed by proton loss from the initially formed C-11 carbenium ion to form (6), followed by reprotonation at C'-2 to give a more stable conjugated carbenium ion. No 1,11-ethano-steroid was obtained.

This reaction pathway was only partly suppressed when (2), the 11 $\alpha$ -ethynyl analogue, was subjected to the same conditions. The major of the two isolated products was identified as 1' $\xi$ -methyl-1,11 $\xi$ -methano-equilenin 3-methyl ether (7), evidently formed by the

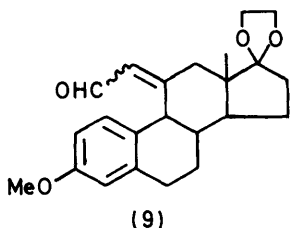


same deprotonation-reprotonation process, followed by ring closure and double bond migration. The minor product proved to be the desired 1,11-etheno-compound (8).

<sup>1</sup> C. G. Pitt, D. H. Rector, D. H. White, M. C. Wani, A. T. McPhail, and R. W. Miller, *J.C.S. Perkin I*, 1976, 2374.

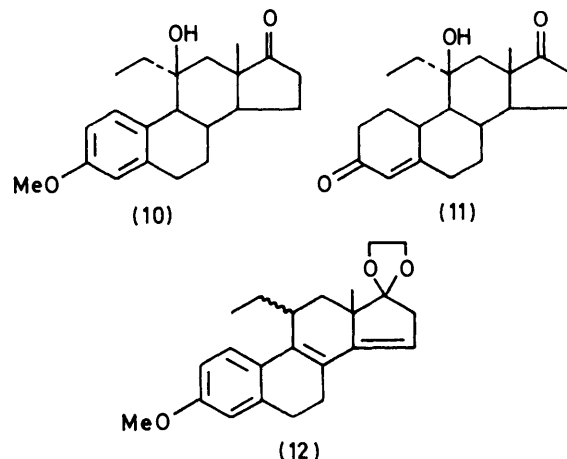
In an attempt to improve the yield of this compound, (1) was subjected to hydroboration. The expected glycol (3) was oxidized to the aldehyde (4) with chromium trioxide in pyridine. Compound (4) represents a latent electrophile which, unlike (1) and (2), can only cyclise at the terminal position of the 11-substituent. Indeed, treatment of (4) with anhydrous hydrogen fluoride did afford the 1,11-etheno-steroid (8), albeit in poor yield.

The best method of synthesis of (8) proved to be treatment of the 11 $\alpha$ -ethynyl-11 $\beta$ -hydroxy-derivative (2) with tris(triphenylsilyl) vanadate. This reagent is reported<sup>2</sup> to isomerise ethynyl carbinols to  $\alpha\beta$ -unsaturated aldehydes and was applied with the expectation of converting (2) into (9), followed by acid-catalysed cyclization. In fact, when (2) was treated with this reagent, the 1,11-etheno-steroid (8) (76%) was obtained directly. The minor products were tentatively identified as the  $\alpha\beta$ -unsaturated aldehyde (9) and its  $\beta\gamma$ -unsaturated isomer(s). This mixture of aldehydes also gave (8) when treated with tris(triphenylsilyl) vanadate,



suggesting they are transient intermediates in the cyclization reaction.

Despite the precedent<sup>3</sup> for reductive alkylation-cyclization of numerous other  $\pi$ -systems, and the demonstrated addition of a carbanion to allyl alcohol,<sup>4</sup> no product with a 1,11-etheno-bridge was isolated.



When (6), derived from dehydration of (1) with  $\text{POCl}_3$  in pyridine, was heated at 173 °C in 1,2-dichlorobenzene containing 5% pyridine, the major product appeared to be the isomeric pentaene (12). No product of cycloaddition of the aromatic and the 11-vinyl groups was detected. If pyridine was omitted from the solvent, (6) was recovered unchanged.

An X-ray single-crystal analysis of (8) confirmed the structural assignment and provided details of the molecular conformation illustrated in Figure 1. Final

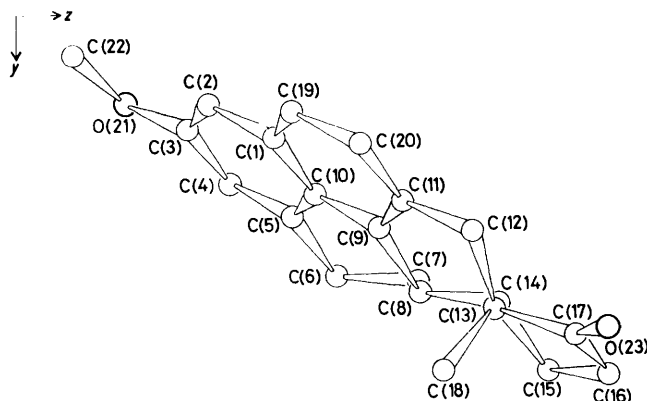


FIGURE 1 Atom numbering scheme and molecular conformation of (8)

Another method of construction of a two-carbon bridge between C(1) and C(11) which was considered was reductive cyclization *via* the benzenoid radical anion of (1). However, the only products isolated from the reduction of (1) with lithium-ammonia-*t*-butanol were the 11 $\alpha$ -ethyl-11 $\beta$ -hydroxy-compounds (10) and (11), formed by independent reduction of the two  $\pi$ -systems.

<sup>2</sup> H. Pauling, *Chimia*, 1973, 27, 383; G. L. Olson, K. D. Morgan, and G. Saucy, *Synthesis*, 1976, 25; G. L. Olson, H.-C. Cheung, K. Morgan, R. Borer, and G. Saucy, *Helv. Chim. Acta*, 1976, 59, 567; H. Pauling, D. A. Andrews, and N. C. Hindley, *ibid.*, p. 1233.

atomic co-ordinates are listed in Tables 1 and 2. Interatomic distances and valency angles involving the non-hydrogen atoms are in Table 3; torsion angles are in Table 4. Displacements of selected atoms from various least-squares planes are in Table 5.

<sup>3</sup> H. O. House, 'Modern Synthetic Reactions,' 2nd edn., Benjamin, Menlo Park, California, pp. 166-172, and references therein.

<sup>4</sup> D. R. Dimmel and J. P. O'Malley, *J. Org. Chem.*, 1975, 40, 132.

steroid skeleton in (8) where the maximum deviation of any ring atom from the least-squares plane through the naphthalene moiety is 0.635 Å for C(7). Mean bond lengths in the naphthalene rings, averaged according

TABLE 1

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

Atom	<i>x</i>	<i>y</i>	<i>z</i>
C(1)	5 930(4)	719(1)	1 344(5)
C(2)	5 145(5)	532(1)	-333(5)
C(3)	3 567(5)	675(1)	-879(5)
C(4)	2 706(4)	1 000(1)	233(5)
C(5)	3 433(4)	1 193(1)	1 830(5)
C(6)	2 508(4)	1 546(1)	2 968(5)
C(7)	3 119(4)	1 569(1)	5 075(5)
C(8)	5 041(4)	1 637(1)	5 117(4)
C(9)	5 933(4)	1 255(1)	4 075(5)
C(10)	5 101(4)	1 058(1)	2 416(5)
C(11)	7 520(4)	1 098(1)	4 669(5)
C(12)	8 408(4)	1 270(1)	6 474(5)
C(13)	7 732(4)	1 723(1)	7 068(5)
C(14)	5 774(4)	1 694(1)	7 148(4)
C(15)	5 231(4)	2 091(1)	8 386(5)
C(16)	6 587(5)	2 115(1)	9 966(5)
C(17)	8 134(5)	1 881(1)	9 142(5)
C(18)	8 390(4)	2 091(1)	5 700(5)
C(19)	7 544(4)	573(1)	1 970(6)
C(20)	8 275(5)	755(1)	3 575(6)
O(21)	2 676(3)	528(1)	-2 479(3)
C(22)	3 561(6)	241(1)	-3 819(6)
O(23)	9 466(4)	1 833(1)	9 966(4)

TABLE 2

Hydrogen atom fractional co-ordinates ( $\times 10^3$ ), isotropic thermal parameters, and distances (*d*) to their bonded carbon atoms, with estimated standard deviations in parentheses

Atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>B</i> /Å <sup>2</sup>	<i>d</i> /Å
H(2)	571(4)	32(1)	-106(5)	3.4(8)	0.93(3)
H(4)	166(5)	109(1)	-30(5)	3.9(7)	0.94(4)
H(6 $\alpha$ )	144(4)	146(1)	289(5)	3.7(7)	0.88(3)
H(6 $\beta$ )	271(4)	188(1)	235(5)	4.0(8)	1.09(3)
H(7 $\alpha$ )	281(4)	132(1)	578(4)	2.0(6)	0.92(3)
H(7 $\beta$ )	252(4)	180(1)	591(5)	3.4(7)	1.01(3)
H(8)	533(4)	192(1)	435(4)	1.7(6)	1.01(3)
H(12 $\alpha$ )	821(4)	104(1)	758(4)	2.3(6)	1.03(3)
H(12 $\beta$ )	955(4)	129(1)	625(4)	2.6(6)	0.91(3)
H(14)	551(3)	144(1)	783(4)	1.7(6)	0.92(3)
H(15 $\alpha$ )	422(3)	205(1)	901(4)	1.6(5)	0.91(3)
H(15 $\beta$ )	520(4)	237(1)	762(4)	2.8(6)	0.99(3)
H(16 $\alpha$ )	625(5)	197(1)	1 103(5)	3.8(8)	0.89(3)
H(16 $\beta$ )	679(4)	241(1)	1 045(4)	2.9(7)	0.95(3)
H(18A)	777(4)	239(1)	596(5)	3.5(7)	1.03(3)
H(18B)	952(4)	213(1)	574(5)	3.9(8)	0.90(3)
H(18C)	821(4)	200(1)	427(5)	3.4(7)	1.02(3)
H(19)	808(5)	35(1)	129(5)	4.0(8)	0.92(3)
H(20)	924(4)	65(1)	393(5)	3.4(7)	0.86(3)
H(22A)	287(5)	23(1)	-484(6)	6.6(11)	0.88(4)
H(22B)	378(5)	-8(1)	-329(6)	5.2(9)	1.05(3)
H(22C)	455(4)	39(1)	-420(5)	3.9(8)	0.94(3)

to  $D_{2h}$  symmetry [C(1)-C(2) 1.424, C(2)-C(3) 1.369, C(3)-C(4) 1.409, C(1)-C(10) 1.415 Å] agree well with the corresponding values in naphthalene (1.425, 1.361, 1.421, and 1.410 Å),<sup>5</sup> 1,8-dimethylnaphthalene (1.425, 1.354, 1.431, and 1.391 Å),<sup>6</sup> and 1*H*,3*H*-naphtho[1,8-*cd*]-thiopyran (1.418, 1.361, 1.395, and 1.430 Å).<sup>7</sup> However, fusion of the naphthalene system to rings B and C in (8) does introduce some strain which is reflected in the small difference between the mean of the C(5)-C(6) and

C(9)-C(10) distances (1.434 Å) compared with that of C(1)-C(2) and C(1)-C(19) (1.414 Å). In addition, whereas the naphthalene moieties and their bonded

TABLE 3

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

(a) Bond lengths			
C(1)-C(2)	1.418(5)	C(9)-C(11)	1.395(4)
C(1)-C(10)	1.415(4)	C(11)-C(12)	1.509(5)
C(1)-C(19)	1.410(5)	C(11)-C(20)	1.407(5)
C(2)-C(3)	1.365(5)	C(12)-C(13)	1.517(4)
C(3)-C(4)	1.410(5)	C(13)-C(14)	1.544(4)
C(3)-O(21)	1.373(4)	C(13)-C(17)	1.528(5)
C(4)-C(5)	1.362(4)	C(13)-C(18)	1.537(5)
C(5)-C(6)	1.504(4)	C(14)-C(15)	1.522(4)
C(5)-C(10)	1.430(4)	C(15)-C(16)	1.520(5)
C(6)-C(7)	1.521(5)	C(16)-C(17)	1.515(5)
C(7)-C(8)	1.526(4)	C(17)-O(23)	1.198(5)
C(8)-C(9)	1.523(4)	C(19)-C(20)	1.354(6)
C(8)-C(14)	1.513(4)	O(21)-C(22)	1.437(5)
C(9)-C(10)	1.438(4)		
(b) Valency angles			
C(2)-C(1)-C(10)	120.2(3)	C(9)-C(11)-C(12)	122.5(3)
C(2)-C(1)-C(9)	121.0(3)	C(9)-C(11)-C(20)	118.1(3)
C(10)-C(1)-C(19)	118.8(3)	C(12)-C(11)-C(20)	119.4(3)
C(1)-C(2)-C(3)	119.5(3)	C(11)-C(12)-C(13)	111.3(3)
C(2)-C(3)-C(4)	120.4(3)	C(12)-C(13)-C(14)	108.0(2)
C(2)-C(3)-O(21)	125.5(3)	C(12)-C(13)-C(17)	117.0(3)
C(4)-C(3)-O(21)	114.0(3)	C(12)-C(13)-C(18)	111.3(3)
C(3)-C(4)-C(5)	121.6(3)	C(14)-C(13)-C(17)	101.0(2)
C(4)-C(5)-C(6)	120.7(3)	C(14)-C(13)-C(18)	113.4(2)
C(4)-C(5)-C(10)	119.3(3)	C(17)-C(13)-C(18)	105.9(2)
C(6)-C(5)-C(10)	119.9(3)	C(8)-C(14)-C(13)	110.8(2)
C(5)-C(6)-C(7)	111.7(3)	C(8)-C(14)-C(15)	119.5(2)
C(6)-C(7)-C(8)	109.7(2)	C(13)-C(14)-C(15)	104.8(2)
C(7)-C(8)-C(9)	110.3(2)	C(14)-C(15)-C(16)	103.7(3)
C(7)-C(8)-C(14)	114.2(2)	C(15)-C(16)-C(17)	106.1(3)
C(9)-C(8)-C(14)	109.8(2)	C(13)-C(17)-C(16)	108.8(3)
C(8)-C(9)-C(10)	118.0(2)	C(13)-C(17)-O(23)	125.5(3)
C(8)-C(9)-C(11)	122.1(3)	C(16)-C(17)-O(23)	125.7(3)
C(10)-C(9)-C(11)	119.9(3)	C(1)-C(19)-C(20)	120.2(3)
C(1)-C(10)-C(5)	118.8(3)	C(11)-C(20)-C(19)	123.2(3)
C(1)-C(10)-C(9)	119.7(3)	C(3)-O(21)-C(22)	117.0(3)
C(5)-C(10)-C(9)	121.5(3)		
(c) Intermolecular separations * < 3.60 Å			
O(23) ... C(6 <sup>I</sup> )	3.27	C(7) ... O(21 <sup>III</sup> )	3.56
C(3) ... C(22 <sup>III</sup> )	3.51	O(23) ... C(4 <sup>I</sup> )	3.58
O(21) ... C(22 <sup>III</sup> )	3.54		

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

$$\begin{array}{ll} \text{I} & 1 + x, y, 1 + z \\ \text{II} & \frac{1}{2} - x, -y, \frac{1}{2} + z \\ \text{III} & x, y, 1 + z \end{array}$$

substituents are planar to within 0.007, 0.02, and 0.025 Å, respectively, in these other three compounds, the carbon atoms defining rings A and E in (8) are planar only to within 0.04 Å. Individual ring A and E atom deviations from their least-squares plane indicate a slight bowing towards the  $\alpha$ -face of the molecule about a line passing through C(2) and C(9), and the substituent atoms C(6), C(8), C(12), and O(21) are displaced significantly from this plane. At the methoxy-substituent the geometry is similar to that found in other com-

<sup>5</sup> D. W. J. Cruickshank, *Acta Cryst.*, 1957, **10**, 504.

<sup>6</sup> D. Bright, I. E. Maxwell, and J. de Boer, *J.C.S. Perkin II*, 1973, 2101.

<sup>7</sup> B.-M. Lundén, *Acta Cryst.*, 1973, **B29**, 1219.

pounds;<sup>8</sup> the small C(2)-C(3)-O(21)-C(22) torsion angle ( $-8.1^\circ$ ), indicates that the methyl group lies close to the aromatic ring plane and the exocyclic valency angles at C(3) display the usual asymmetry.

The observed bowing of the naphthalene moiety and

TABLE 4

Torsion angles ( $^\circ$ ), with estimated standard deviations in parentheses; the angle A-B-C-D is defined as positive, when viewed along the B-C bond, atom A must be rotated clockwise to eclipse atom D

C(10)-C(1)-C(2)-C(3)	-1.4(3)
C(19)-C(1)-C(2)-C(3)	178.8(4)
C(2)-C(1)-C(10)-C(5)	2.8(3)
C(2)-C(1)-C(10)-C(9)	-178.0(3)
C(19)-C(1)-C(10)-C(5)	-177.4(3)
C(19)-C(1)-C(10)-C(9)	1.8(3)
C(2)-C(1)-C(19)-C(20)	180.0(4)
C(10)-C(1)-C(19)-C(20)	0.3(4)
C(1)-C(2)-C(3)-C(4)	-1.2(4)
C(1)-C(2)-C(3)-O(21)	179.0(4)
C(2)-C(3)-C(4)-C(5)	2.5(4)
O(21)-C(3)-C(4)-C(5)	-177.7(3)
C(2)-C(3)-O(21)-C(22)	-8.1(3)
C(4)-C(3)-O(21)-C(22)	172.1(3)
C(3)-C(4)-C(5)-C(6)	178.6(3)
C(3)-C(4)-C(5)-C(10)	-1.0(3)
C(4)-C(5)-C(6)-C(7)	154.9(3)
C(10)-C(5)-C(6)-C(7)	-25.5(3)
C(4)-C(5)-C(10)-C(1)	-1.6(3)
C(4)-C(5)-C(10)-C(9)	179.2(3)
C(6)-C(5)-C(10)-C(1)	178.8(3)
C(6)-C(5)-C(10)-C(9)	-0.4(3)
C(5)-C(6)-C(7)-C(8)	55.2(3)
C(6)-C(7)-C(8)-C(9)	-59.4(3)
C(6)-C(7)-C(8)-C(14)	176.4(3)
C(7)-C(8)-C(9)-C(10)	34.2(3)
C(7)-C(8)-C(9)-C(11)	-146.5(3)
C(14)-C(8)-C(9)-C(10)	161.0(3)
C(14)-C(8)-C(9)-C(11)	-19.8(3)
C(7)-C(8)-C(14)-C(13)	175.4(3)
C(7)-C(8)-C(14)-C(15)	-62.7(3)
C(9)-C(8)-C(14)-C(13)	50.9(3)
C(9)-C(8)-C(14)-C(15)	172.8(3)
C(8)-C(9)-C(10)-C(1)	176.5(3)
C(8)-C(9)-C(10)-C(5)	-4.3(3)
C(11)-C(9)-C(10)-C(1)	-2.8(3)
C(11)-C(9)-C(10)-C(5)	176.4(3)
C(8)-C(9)-C(11)-C(12)	4.9(3)
C(8)-C(9)-C(11)-C(20)	-177.7(3)
C(10)-C(9)-C(11)-C(12)	-175.9(3)
C(10)-C(9)-C(11)-C(20)	1.5(3)
C(9)-C(11)-C(12)-C(13)	-20.9(3)
C(20)-C(11)-C(12)-C(13)	161.7(3)
C(9)-C(11)-C(20)-C(19)	0.6(4)
C(12)-C(11)-C(20)-C(19)	178.2(4)
C(11)-C(12)-C(13)-C(14)	50.4(3)
C(11)-C(12)-C(13)-C(17)	163.4(3)
C(11)-C(12)-C(13)-C(18)	-74.7(3)
C(12)-C(13)-C(14)-C(8)	-68.7(3)
C(12)-C(13)-C(14)-C(15)	161.2(2)
C(17)-C(13)-C(14)-C(8)	168.0(2)
C(17)-C(13)-C(14)-C(15)	37.9(3)
C(18)-C(13)-C(14)-C(8)	55.2(3)
C(18)-C(13)-C(14)-C(15)	-74.9(3)
C(12)-C(13)-C(17)-C(16)	-140.7(3)
C(12)-C(13)-C(17)-O(23)	40.7(4)
C(14)-C(13)-C(17)-C(16)	-23.8(3)
C(14)-C(13)-C(17)-O(23)	157.6(4)
C(18)-C(13)-C(17)-C(16)	94.7(3)
C(18)-C(13)-C(17)-O(23)	-84.0(4)
C(8)-C(14)-C(15)-C(16)	-163.0(3)
C(13)-C(14)-C(15)-C(16)	-38.2(3)
C(14)-C(15)-C(16)-C(17)	22.6(3)
C(15)-C(16)-C(17)-C(13)	1.1(3)
C(15)-C(16)-C(17)-O(23)	179.8(4)
C(1)-C(19)-C(20)-C(11)	-1.6(4)

the out-of-plane displacements of the carbon substituents appear to occur principally in order to minimize the  $\beta$ -face 1,3-diaxial non-bonded H(8)  $\cdots$  C(18) methyl group interaction through outward rotation of the C(8)-H(8) and C(13)-C(18) bonds. Further consequences of this rotation are the departures of ring B, constrained to maintain two adjacent torsion angles at nearly  $0^\circ$ , and ring C, with only one such constraint, from their respective Dreiding molecular model conformations of C(7)  $\alpha$ -envelope and intermediate half-chair, C(14)  $\alpha$ -envelope forms. The experimentally

TABLE 5

Equations of least-squares planes in the form  $AX + BY + CZ + D = 0$ , where  $X$ ,  $Y$ , and  $Z$  are orthogonal Å coordinates; displacements (Å) of relevant atoms from the planes are in square brackets

Plane (A): C(1)-(11), C(19), C(20)

$$0.420 8X + 0.695 5Y - 0.582 4Z - 2.924 = 0$$

$$[C(1) 0.006, C(2) 0.024, C(3) 0.017, C(4) -0.032, C(5) -0.024, C(6) -0.046, C(7) -0.635, C(8) 0.128, C(9) 0.040, C(10) 0.013, C(11) 0.001, C(12) -0.065, C(13) 0.421, C(14) -0.319, C(15) -0.164, C(16) -0.293, C(17) 0.056, C(18) 1.951, C(19) -0.013, C(20) -0.031, O(21) 0.052, C(22) 0.279]$$

Plane (B): C(5), C(6), C(9), C(10)

$$0.394 7X + 0.702 5Y - 0.592 2Z - 2.840 = 0$$

$$[C(5) 0.002, C(6) -0.001, C(7) -0.615, C(8) 0.108, C(9) 0.001, C(10) -0.002]$$

Plane (C): C(8), C(9), C(11), C(12)

$$0.472 5X + 0.670 3Y - 0.572 2Z - 3.159 = 0$$

$$[C(8) 0.010, C(9) -0.021, C(11) 0.021, C(12) -0.010, C(13) 0.419, C(14) -0.398]$$

Plane (D): C(13), C(15)-(17), O(23)

$$0.323 3X + 0.871 1Y - 0.369 8Z - 4.684 = 0$$

$$[C(13) 0.004, C(14) -0.589, C(15) -0.004, C(16) 0.006, C(17) -0.007, O(23) 0.000]$$

determined unequal C(7) and C(8) displacements ( $-0.615$  and  $0.108$  Å) from the least-squares plane through C(5), C(6), C(9), and C(10) indicate that ring B approximates to a C(7)  $\alpha$ -envelope form but is distorted slightly towards a half-chair form. Analysis of the deviations of the endocyclic torsion angles from their ideal symmetry-constrained values [ $\Delta(C_s-E)$  17.6,  $\Delta(C_2-HC)$  42.6°\*] confirms the appropriateness of this description of the ring conformation. Atoms C(13) and C(14) are displaced by approximately equal amounts (0.419 and 0.398 Å) to the  $\beta$ - and  $\alpha$ -sides of the least-squares plane through the remaining ring C atoms and, accordingly, the ring is very close to a half-chair conformation [ $\Delta(C_s-E)$  73.0,  $\Delta(C_2-HC)$  6.5°].†

X-Ray structural investigations on 17-oxo-steroids have demonstrated that a variety of ring D forms exist

\* For ring B,  $\Delta(C_s-E) = |\omega_{5,10}| + |\omega_{9,10}| + |\omega_{5,6} + \omega_{8,9}| + |\omega_{6,7} + \omega_{7,8}|$ ,  $\Delta(C_2-HC) = |\omega_{5,10}| + |\omega_{5,6} - \omega_{9,10}| + |\omega_{6,7} - \omega_{8,9}|$ , where  $\omega_{i,j}$  is the endocyclic torsion angle about the C(i)-C(j) bond.

† For ring C,  $\Delta(C_s-E) = |\omega_{8,9}| + |\omega_{9,11}| + |\omega_{8,14} + \omega_{11,12}| + |\omega_{12,13} + \omega_{13,14}|$ ,  $\Delta(C_2-HC) = |\omega_{9,11}| + |\omega_{8,9} - \omega_{11,12}| + |\omega_{8,14} - \omega_{12,13}|$ .

<sup>8</sup> P. Coggon, A. T. McPhail, and S. C. Wallwork, *J. Chem. Soc. (B)*, 1970, 884, and references therein.

even in very closely related structures.<sup>9,10</sup> Thus, it may be concluded that this ring is very flexible and the observed solid-state conformation will depend to some extent on crystal packing forces. Of particular interest

TABLE 6

Comparison of parameters defining some estrone D-ring conformations with ideal forms

C(14)	$\Delta(C_2 - E)^a$	$\Delta(C_2 - HC)^e$	$\Delta^a$	$\phi_m^a$
$\alpha$ -envelope <sup>a</sup>	0	44.4	-36.0	46.7
Compound (8)	2.6	35.9	-34.2	39.7
4-Bromoestrone <sup>b</sup>	4.8	36.3	-39.9	42.4
Estrone IIIB <sup>c</sup>	10.6	42.8	-30.0	41.0
Estrone I <sup>c</sup>	19.5	22.1	-19.6	41.6
Estrone II <sup>c</sup>	24.0	18.7	-16.2	43.1
Estrone IIIA <sup>c</sup>	34.0	6.9	-6.3	40.9
C(13 $\beta$ ), C(14 $\alpha$ ) half-chair <sup>a</sup>	46.7	0	0	46.9

<sup>a</sup> C. Altona, H. J. Geise, and C. Romers, *Tetrahedron*, 1968, 24, 13. <sup>b</sup> D. Norton, G. Kartha, and C. T. Lu, *Acta Cryst.*, 1963, 16, 89. <sup>c</sup> Ref. 7. <sup>d</sup>  $\Delta(C_2 - E) = |\omega_{16,17}| + |\omega_{13,17} + \omega_{15,16}| + |\omega_{13,14} + \omega_{14,15}|$ , where  $\omega_{i,j}$  is the endocyclic torsion angle around the C(i) - C(j) bond. <sup>e</sup>  $\Delta(C_2 - HC) = |\omega_{15,16} - \omega_{16,17}| + |\omega_{13,17} - \omega_{14,15}|$ .

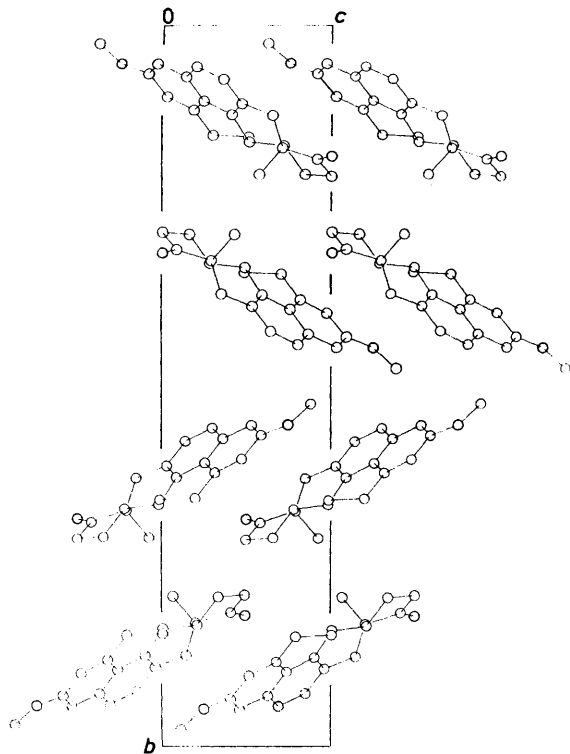


FIGURE 2 Packing of molecules of (8) in the crystal, viewed in projection along the *a* axis

with regard to the present study are the different conformations found for ring D in estrone polymorphs<sup>11</sup> and characterized by the parameters in Table 6. In each of these crystals there exist relatively strong

<sup>9</sup> C. Romers, C. Altona, H. J. C. Jacobs, and R. A. DeGraff, in 'Terpenoids and Steroids,' ed. K. H. Overton, Specialist Periodical Reports, Chemical Society, London, vol. 4, 1973.

<sup>10</sup> W. L. Duax, C. M. Weeks, and D. C. Rohrer, *Topics in Stereochem.*, 1976, 9, 271.

hydrogen-bonded interactions which would certainly be expected to influence significantly the observed conformations.<sup>12</sup> The packing of molecules of (8) in the crystal as viewed in projection along the *a* axis is shown in Figure 2. The shortest intermolecular separations (Table 3) are typical of weak van der Waals type interactions, and it is of interest to note that ring D consequently adopts an almost ideal C(14)  $\alpha$ -envelope form.

The uterotropic activity (rat, s.c.) of 3-hydroxy-1,11-ethenoestra-1,3,5(10),9(11)-tetraen-17-one, derived from demethylation of (8), was 0.5% of that of estrone.

#### EXPERIMENTAL

M.p.s were determined using a Kofler-hot-stage microscope. I.r. spectra were measured with a Perkin-Elmer 267 spectrophotometer. Unless otherwise mentioned, n.m.r. spectra were recorded on a Varian HA 100, with tetramethylsilane as an internal standard; chemical shifts are expressed in  $\delta$  units. Mass spectra were determined on an A.E.I. MS 902. U.v. spectra were obtained by use of a Cary 14 spectrophotometer. G.l.c. analysis was carried out on a Varian 1400 instrument with a column containing 3% Se-30 on Variport. Most reactions were carried out under dry, oxygen-free nitrogen.

17,17-Ethylenedioxy-11 $\alpha$ -ethynyl-3-methoxyestra-1,3,5(10)-trien-11 $\beta$ -ol (2).—17,17-Ethylenedioxy-3-methoxy-1,3,5(10)-trien-11-one<sup>1</sup> (1.74 g, 5.08 mmol) was added to a solution of lithium acetylide, prepared by adding *n*-butyl-lithium in hexane (20.3 ml, 2.5M) to a saturated solution of acetylene in tetrahydrofuran (150 ml) at  $-78^\circ\text{C}$ . After 1 h, the reaction mixture was allowed to warm to room temperature, quenched with saturated ammonium chloride, poured into diethyl ether (500 ml), washed (water and brine), and dried ( $\text{Na}_2\text{SO}_4$ ). Concentration and crystallization gave (2) (1.30 g, 70%). The mother liquor (0.48 g) was chromatographed on silica gel (50 g). Ether-hexane (3:7) eluted the 11 $\beta$ -ol (2) (0.154 g; total yield 77%), m.p.  $194-197^\circ\text{C}$  (ether-hexane);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 3540 (OH), 3300 (*H-C*:C-), and 1605 and 1570  $\text{cm}^{-1}$  (aromatic);  $\delta$  ( $\text{CDCl}_3$ ) 1.05 (3 H, s, C-18), 2.65 (1 H, s, *H-C*:C-), 3.73 (3 H, s, MeO), 3.88 (4 H, s, O- $\text{CH}_2$ - $\text{CH}_2$ -O), 6.6 (2 H, m, C-2 and C-4), and 8.4 (1 H, d, *J* 8 Hz, C-1); (Found:  $M^+$ , 368.199.  $\text{C}_{23}\text{H}_{28}\text{O}_4$  requires  $M^+$ , 368.199).

3-Methoxy-1,11-ethenoestra-1,3,5(10),9(11)-tetraen-17-one (8).—A mixture of (2) (0.795 g, 2.16 mmol), tris(triphenylsilyl) vanadate (0.193 g, 0.216 mmol), triphenylsilylanol (0.0596 g, 0.216 mmol), and benzoic acid (0.06 g) was heated under reflux in xylene (30 ml) for 21 h. After cooling, hexane (100 ml) was added and the precipitate filtered off, washed (10% NaOH, water, and brine), and concentrated. The residue was taken up in 1:1 methanol-ether (20 ml) containing 10% hydrochloric acid (2 ml). After 1 h, work-up in the usual way followed by crystallization from diethyl ether-hexane gave the etheno-derivative (8) (0.289 g, 44%). The mother liquor was chromatographed on silica gel (75 g). Carbon tetrachloride-chloroform (7:3) eluted (8) (0.213 g; total yield 76%), m.p.  $180-183^\circ\text{C}$  (diethyl ether-hexane);  $\nu_{\text{max}}$  (KBr) 1735 (CO) and 1615 and 1598  $\text{cm}^{-1}$  (aromatic);  $\lambda_{\text{max}}$  (MeOH)

<sup>11</sup> B. Busetta, C. Courseille, and M. Hospital, *Acta Cryst.*, 1973, B29, 298.

<sup>12</sup> See e.g. A. T. McPhail, P. A. Luhan, P. S. W. Tschang, and K. D. Onan, *J.C.S. Perkin II*, 1977, 379; P. A. Luhan and A. T. McPhail, *ibid.*, 1973, 51.

234 ( $\epsilon$  69 000), 268 (4 500), 277 (5 100), 287 (3 400), and 337 nm (2 900);  $\delta$  ( $\text{CDCl}_3$ ) 0.98 (3 H, s, C-18), 2.92br (2 H, s, C-12), 3.87 (3 H, s, MeO), 6.94br (2 H, s, C-2 and C-4), 7.17, and 7.52 (2 H, ABq,  $J$  8 Hz, C-1' and C-2'); (Found:  $M^+$ , 306.162.  $\text{C}_{21}\text{H}_{22}\text{O}_2$  requires  $M^+$ , 306.162).

*Acid-catalysed Cyclization of the 11 $\beta$ -Ol* (2).—A mixture of (2) (0.500 g, 1.36 mmol) and toluene-*p*-sulphonic acid monohydrate (0.500 g) in benzene (70 ml) was heated under reflux for 1 h, water being removed with a Dean-Stark separator. Water (3 ml) was added and the mixture stirred at room temperature for 0.5 h. It was then diluted with diethyl ether, washed (saturated  $\text{NaHCO}_3$ ,  $\text{H}_2\text{O}$ , and brine), dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated. The residue (0.224 g) was chromatographed on silica gel (two EM prepacked columns, size B). Elution with chloroform-carbon tetrachloride (3:7) gave three homogeneous fractions (A)–(C), characterized as follows.

(a) 3-Methoxy-1'-methyl-1,11 $\xi$ -methanoestra-1,3,5(10),6,8-pentaen-17-one (7). Crystallization of fraction (A) (0.029 g, 7%) from diethyl ether-hexane gave the *methano-steroid* (7), m.p. 203–205 °C;  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 1 740 (CO) and 1 605  $\text{cm}^{-1}$  (aromatic);  $\lambda_{\text{max}}$  (MeOH) 237 nm ( $\epsilon$  64 600);  $\delta$  ( $\text{CDCl}_3$ ) 0.47 (3 H, s, C-18), 1.65 (3 H, d,  $J$  7 Hz, 1'-Me), 3.72 (3 H, s, MeO), 6.87 (2 H, m, C-2 and C-4), and 7.22 and 7.47 (2 H, ABq,  $J$  8 Hz, C-6 and C-7) (Found:  $M^+$ , 306.162.  $\text{C}_{21}\text{H}_{22}\text{O}_2$  requires  $M^+$ , 306.162).

(b) Crystallization of (B) (0.01 g, 3%) from diethyl ether-hexane gave (8).

(c) Fraction (C) (0.052 g, 12%) was identified as the 17-ketone analogue of (2);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 3 670s and 3 550br (OH), 3 300 ( $\text{H}\cdot\text{C}\cdot\text{C}\cdot$ ), 1 735 (CO), and 1 605 and 1 570  $\text{cm}^{-1}$  (aromatic);  $\delta$  ( $\text{CDCl}_3$ ) 1.05 (3 H, s, C-18), 2.65 (1 H, s,  $\text{H}\cdot\text{C}\cdot\text{C}\cdot$ ), 3.72 (3 H, s, MeO), 6.52 (2 H, m, C-2 and C-4), and 8.37 (1 H, d,  $J$  8 Hz, C-1).

17,17-Ethylenedioxy-11 $\alpha$ -(2-hydroxyethyl)-3-methoxyestra-1,3,5(10)-trien-11 $\beta$ -ol (3).—Diborane in tetrahydrofuran (2.76 ml, 0.98M) was added to a stirred solution of (1) (0.200 g, 0.540 mmol) in tetrahydrofuran (20 ml). After 1.75 h, ethanol (1 ml), 10% NaOH (1 ml), and 30%  $\text{H}_2\text{O}_2$  (0.5 ml) were cautiously added. The reaction mixture was heated under reflux for 1 h, diluted with water, and extracted with diethyl ether. The organic phase was worked up in the usual way. The product was purified by p.t.l.c. (silica gel, 20  $\times$  40  $\times$  0.1 cm; ether-hexane, 4:6) to give (3) (0.093 g);  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 3 600 and 3 500 (OH) and 1 610 and 1 500  $\text{cm}^{-1}$  (aromatic);  $\lambda_{\text{max}}$  (MeOH) 224 ( $\epsilon$  7 200), 276 (1 700), and 282 nm (1 660);  $\delta$  ( $\text{CDCl}_3$ ) 1.08 (3 H, s, C-18), 3.75 (3 H, s, MeO), 3.89 (4 H, s,  $\text{OCH}_2\text{CH}_2\text{O}$ ), 6.57 (2 H, m, C-2 and C-4), and 7.77 (1 H, d,  $J$  8 Hz, C-1); (Found:  $M^+$ , 388.225.  $\text{C}_{23}\text{H}_{32}\text{O}_5$  requires  $M^+$ , 388.225).

17,17-Ethylenedioxy-3-methoxy-11 $\alpha$ -(2-oxoethyl)estra-1,3,5(10)-trien-11 $\beta$ -ol (4).—To a stirred solution of anhydrous chromium trioxide (0.309 g, 3.09 mmol) and pyridine (0.488 g, 6.18 mmol) in methylene chloride (10 ml) was added (7) (0.100 g, 0.258 mmol). After 0.25 h, the reaction was worked up in the usual way to give (4) (0.068 g) as a viscous gum;  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 3 520 (OH), 2 820, 2 720 (CHO), 1 720 (CO), and 1 610  $\text{cm}^{-1}$  (aromatic);  $\delta$  ( $\text{CDCl}_3$ ) 1.1 (3 H, s, C-18), 3.73 (3 H, s, MeO), 3.86 (4 H, brs,  $\text{OCH}_2\text{CH}_2\text{O}$ ), 6.68 (2 H, m, C-2 and C-4), 7.74 (1 H, d,  $J$  9 Hz, C-1), and 9.90br (1 H, s, CHO) (Found:  $M^+$ , 386.209.  $\text{C}_{23}\text{H}_{30}\text{O}_5$  requires  $M^+$ , 386.209).

*Acid-catalysed Cyclization of the Aldehyde* (9).—Anhydrous hydrogen fluoride (2 ml) was added to (9) (0.010 g, 0.0259 mmol) at 0 °C. After 0.5 h at 0°, the mixture was allowed

to warm to room temperature (0.5 h), poured into ice, made basic with 50% sodium hydroxide, and extracted with diethyl ether. The extract was washed (water and brine), dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated. The product was purified by p.t.l.c. (silica gel, 20  $\times$  20  $\times$  0.1 cm; diethyl ether-hexane, 4:6), to give a product (0.68 mg) shown by g.l.c. and t.l.c. to be identical to (8);  $\lambda_{\text{max}}$  (MeOH) 233 nm ( $\epsilon$  12 500). An increase in reaction time (2.5 h) did not increase the yield of (8).

*Birch Reduction of the Olefin* (1).—Lithium metal (0.0643 g, 9.19 mg atom) was added to a stirred solution of (1) (0.200 g, 0.541 mmol) in dry tetrahydrofuran (2 ml), dry *t*-butanol (2 ml), and ammonia (10 ml). After 2.5 h, the deep blue colour of the reaction mixture was discharged with saturated ammonium chloride, and the ammonia evaporated by a stream of nitrogen. Water (10 ml) was added and the mixture extracted with diethyl ether. The extract was washed (water and brine), dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated. This residue was dissolved in methanol-diethyl ether (2:1, 21 ml) containing 10% hydrochloric acid (1.4 ml). After 0.5 h, the product (0.618 g) was isolated in the usual way and chromatographed on silica gel (20 g). Elution with diethyl ether-hexane (3:7) gave two fractions: (A) (0.019 g, 11.2%) and (B) (0.047 g). Crystallization of (A) from diethyl ether-hexane gave 11 $\alpha$ -ethyl-11 $\beta$ -hydroxy-3-methoxyestra-1,3,5(10)-trien-17-one (10), m.p. 123–125 °C;  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 3 590s (OH), 1 738 (CO), and 1 605  $\text{cm}^{-1}$  (aromatic);  $\lambda_{\text{max}}$  (MeOH) 223 ( $\epsilon$  8 600), 277 (1 700), and 282 nm (1 500);  $\delta$  ( $\text{CDCl}_3$ ) 0.97 (3 H, t,  $J$  7 Hz,  $\text{CH}_3\text{-CH}_2\text{-}$ ), 1.08 (3 H, s, C-18), 3.75 (3 H, s, MeO), 6.65 (2 H, m, C-2 and C-4), and 7.58 (1 H, d,  $J$  8 Hz, C-1);  $m/e$  328 ( $M^+$ ), 310 ( $M^+ - 18$ ), 299 ( $M^+ - 29$ ) (Found:  $M^+$ , 328.204.  $\text{C}_{21}\text{H}_{28}\text{O}_3$  requires  $M^+$ , 328.204).

When fraction (B) was rechromatographed on silica gel (5 g), diethyl ether-hexane (1:1) eluted 11 $\alpha$ -ethyl-11 $\beta$ -hydroxyestr-4-ene-3,17-dione (11) (0.020 g, 12%). Although homogeneous (t.l.c. and g.l.c.), attempts to crystallize (11) were unsuccessful;  $\nu_{\text{max}}$  ( $\text{CHCl}_3$ ) 3 600s, 3 460br (OH), and 1 740 and 1 670  $\text{cm}^{-1}$  (CO);  $\lambda_{\text{max}}$  (MeOH) 240 nm ( $\epsilon$  11 400);  $\delta$  ( $\text{CDCl}_3$ ) 0.93 (3 H, t,  $J$  8 Hz,  $\text{CH}_3\text{-CH}_2\text{-}$ ), 1.13 (3 H, s, C-18), and 5.8 (1 H, s, C-4);  $m/e$  316 ( $M^+$ ), 298 ( $M^+ - 18$ ), and 287 ( $M^+ - 29$ ) (Found:  $M^+$ , 316.204.  $\text{C}_{20}\text{H}_{26}\text{O}_3$  requires  $M^+$ , 316.204).

17,17-Ethylenedioxy-3-methoxy-11-vinylestra-1,3,5(10)-9(11)-tetraene (6).—A solution of (1) (0.300 g, 0.811 mmol) and phosphoryl chloride (1.49 g, 9.74 mmol) in pyridine (9 ml) was heated at 50 °C for 28 h. After cooling, the mixture was diluted with diethyl ether, washed (water and brine), and dried ( $\text{Na}_2\text{SO}_4$ ). Concentration gave the *estratetraene* (6) (0.221 g, 77.5%). Although homogeneous (t.l.c. and g.l.c.), attempts to crystallize (6) were unsuccessful;  $\nu_{\text{max}}$  ( $\text{CCl}_4$ ) 1 600  $\text{cm}^{-1}$  (aromatic);  $\lambda_{\text{max}}$  (MeOH) 222 ( $\epsilon$  14 700) and 289 nm (18 300);  $\delta$  ( $\text{CDCl}_3$ ) 0.88 (3 H, s, C-18), 3.77 (3 H, s, MeO), 3.93 (4 H, s,  $\text{O-CH}_2\text{CH}_2\text{-O}$ ), 4.93 (1 H, dd,  $J$  2, 10 Hz,  $\text{HHC}\cdot\text{CH}$ ), 5.17 (1 H, dd,  $J$  2, 17 Hz,  $\text{HHC}\cdot\text{C}(\text{H})$ ), 6.67 (3 H, m, C-2, C-4,  $\text{H}_2\text{C}\cdot\text{CH}$ ), and 7.13 (1 H, d,  $J$  8 Hz, C-1) (Found:  $M^+$ , 352.204.  $\text{C}_{23}\text{H}_{28}\text{O}_3$  requires  $M^+$ , 352.204).

*Attempted Cyclization of the Vinyl-tetraene* (6).—A solution of (6) (0.096 g, 0.274 mmol) in 1,3-dichlorobenzene (15 ml) containing pyridine (0.75 ml) was refluxed for 71 h. Concentration and chromatography on silica gel (EM prepacked column B), and elution with chloroform-carbon tetrachloride (3:7), yielded (12) (0.0199 g, 21%). Although homogeneous (g.l.c. and t.l.c.), the n.m.r. spectrum

of the product showed that it was a mixture;  $\nu_{\max}$  (CCl<sub>4</sub>) 1 605 cm<sup>-1</sup> (aromatic);  $\lambda_{\max}$  (MeOH) 233 ( $\epsilon$  11 900), 297 (12 900), 306 (16 600), and 318 nm (12 400);  $\delta$  (CDCl<sub>3</sub>) 0.80 (3 H, t,  $J$  8 Hz, CH<sub>3</sub>-CH<sub>2</sub>-), 0.98 (3 H, s, C-18), 3.78 (3 H, s, MeO), 3.97 (4 H, s, OCH<sub>2</sub>CH<sub>2</sub>O), 5.61 (1 H, t,  $J$  2 Hz, C-15), 6.72 (2 H, m, C-2 and C-4), and 7.13 and 7.19 (1 H, d,  $J$  10 Hz, C-1) (Found:  $M^+$ , 352.204. Calc. for C<sub>23</sub>H<sub>28</sub>O<sub>3</sub>:  $M^+$ , 352.204).

*3-Hydroxy-1,11-ethenoestra-1,3,5(10),9(11)-tetraen-17-one.*

—Boron tribromide in methylene chloride (4.32 ml, 0.527M) was added to a solution of (8) (0.174 g, 0.569 mmol) in methylene chloride (10 ml) at -78 °C. After warming to room temperature (1 h), the mixture was poured into ice and extracted with methylene chloride. The extract was washed (5% Na<sub>2</sub>SO<sub>3</sub>, water, and brine), dried (Na<sub>2</sub>SO<sub>4</sub>), and concentrated. The residue (0.162 g) was chromatographed on silica gel (16 g). Elution with chloroform-carbon tetrachloride (7:3) gave the product (0.153 g, 92%), m.p. 244—247 °C (decomp.);  $\nu_{\max}$  (KBr) 3 315 (OH), 1 720 (CO), 1 620, 1 600, and 1 580 cm<sup>-1</sup> (aromatic);  $\lambda_{\max}$  (MeOH) 232 ( $\epsilon$  66 200), 267 (3 800), 278 (4 700), 290 (3 200), 332 nm (1 600);  $\delta$  (deuteriodimethyl sulphoxide) 0.85 (3 H, s, C-18), 6.87 (2 H, m, C-2 and C-4), and 7.08 and 7.42 (2 H, ABq,  $J$  8 Hz, C-1' and C-2') (Found:  $M^+$ , 292.146. C<sub>20</sub>H<sub>26</sub>O<sub>2</sub> requires  $M^+$ , 292.146).

*Crystal Data for (8).*—C<sub>21</sub>H<sub>22</sub>O<sub>2</sub>,  $M = 306.4$ . Orthorhombic,  $a = 7.867(5)$ ,  $b = 30.036(20)$ ,  $c = 6.838(5)$  Å,  $U = 1 615.8$  Å<sup>3</sup>,  $D_m$  (floatation) = 1.29,  $Z = 4$ ,  $D_c = 1.259$  g cm<sup>-3</sup>,  $F(000) = 656$ . Cu- $K_{\alpha}$  radiation,  $\lambda = 1.5418$  Å,  $\mu$  (Cu- $K_{\alpha}$ ) = 6.3 cm<sup>-1</sup>. Space group  $P2_12_12_1$  ( $D_2^4$ ) from systematic absences:  $h00$  when  $h \neq 2n$ ,  $0k0$  when  $k \neq 2n$ ,  $00l$  when  $l \neq 2n$ .

*Crystallographic Measurements.*—Initial unit-cell dimensions were obtained from oscillation and Weissenberg photographs taken with Cu- $K_{\alpha}$  radiation for a crystal of dimensions ca.  $0.26 \times 0.30 \times 0.70$  mm, which was then transferred to an Enraf-Nonius CAD 3 automated diffractometer (Ni-filtered Cu- $K_{\alpha}$  radiation, 3° take-off angle), and oriented to rotate with the crystallographic  $c$ -axis parallel to the instrument  $\phi$ -axis. Refined unit-cell constants were obtained by least-squares treatment of the  $\theta$ ,  $\chi$ , and  $\phi$  angles for 40 high-order reflections widely separated in reciprocal space. One octant of data to  $\theta$  67° was collected by the  $\theta$ — $2\theta$  scanning procedure with scanwidths  $(1.20 + 0.60 \tan \theta)^\circ$ . Background measurements were made at each end of the scan range for times equal to half the duration of the scan. A strong standard reflection, checked periodically throughout the data collection, was found to show no significant variation. Of the 1 714 reflections measured, 1 283 were found to have  $I > 2.0\sigma(I)$  [where  $\sigma(I) = (\text{scan count} + \text{total background count})^{1/2}$ ]. Absorp-

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

sorption corrections, determined from the  $\phi$ -dependence of the 004 reflection measured at  $\chi$  90°, were applied to these data which were then corrected for the usual Lorentz and polarization effects.

*Structure Analysis.*—The structure was solved by direct phasing methods using MULTAN<sup>13</sup> with the highest 248  $|E|$  values. The programme was allowed to select five reflections in addition to the three origin-defining reflections; phases for two other reflections obtained from the  $\Sigma_1$  relationship aided in the subsequent phasing calculations. An  $E$  map calculated with the set of phases having the lowest residual and highest figure-of-merit revealed positions for all non-hydrogen atoms. Positional and isotropic thermal parameters were refined by full-matrix least-squares calculations to  $R$  0.116 at which point hydrogen atom positions were located in a difference-Fourier synthesis. Further least-squares refinement of the positional and thermal parameters (anisotropic for carbon and oxygen, isotropic for hydrogen) brought the refinement to convergence at  $R$  0.044. Final atomic positional and isotropic thermal parameters are in Tables 1 and 2. Anisotropic temperature factor parameters for non-hydrogen atoms and valency angles involving hydrogen atoms have been deposited with observed and calculated structure amplitudes as Supplementary Publication No. SUP 21932 (12 pp., 1 microfiche).\*

Atomic scattering factors used in all the structure-factor calculations were those for oxygen and carbon from ref. 14 and for hydrogen from ref. 15. In the least-squares calculations  $\Sigma w\Delta^2$  was minimized; the weighting scheme,  $\sqrt{w} = 1$  for  $|F_o| \leq 14.0$  and  $\sqrt{w} = 14.0/|F_o|$  for  $|F_o| > 14.0$ , showed only random variations of  $\Sigma w\Delta^2$  when analysed in ranges of  $|F_o|$ .

Financial support of part of this work by the contractive Development Branch, Centre for Population Research (N.I.C.H.D., N.I.H.) is hereby acknowledged. We thank Dr. J. S. Baran, Searle Laboratories, for a gift of 17,17-ethylenedioxyestra-1,3,5(10)-triene-3,11 $\beta$ -diol, Dr. G. L. Olson, Hoffmann-LaRoche, for a gift of tris(triphenylsilyl vanadate), and Dr. H. K. Kim, N.I.C.H.D., for helpful discussions. Crystallographic calculations were performed on an I.B.M. 370/165 computer at Triangle Universities Computation Centre, Research Triangle Park, North Carolina, and supported by a grant of computer time from Duke University. We thank the U.S. National Science Foundation for funds toward purchase of a diffractometer.

[6/1576 Received, 10th August, 1976]

<sup>13</sup> G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

<sup>14</sup> D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1968, **18**, 104.

<sup>15</sup> R. F. Stewart, E. R. Davidson, and W. T. Simpson, *J. Chem. Phys.*, 1965, **42**, 3175.