Tetrahedron. Vol. 28, pp. 1411 to 1425. Pergamon Press 1972. Printed in Great Britain

TETRACYCLIC 1,6-METHANO-[10]ANNULENES

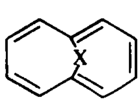
A NOVEL CLASS OF STEROIDAL ANNULENES*

P. H. Bentley,† M. Todd‡, W. McCrae, M. L. Maddox and J. A. Edwards
Institute of Organic Chemistry, Syntex Research, Palo Alto, California

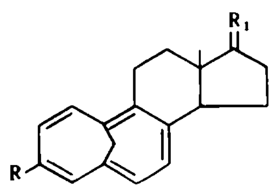
(*Received in the USA* 15 *November* 1971; *Received in the UK for publication* 19 *November* 1971)

Abstract—Reaction of 19-hydroxyandrosta-4,6-diene-3,17-dione (**8b**) and the corresponding Δ^7-compound (**8c**) with diethyl-(2-chloro-1,1,2-trifluoroethyl)-amine affords 5β,19-cyclo-$\Delta^{1,6}$- and 5β,19-cyclo-$\Delta^{1,7}$-3-ketones (**4b**) and (**4c**) respectively. Solvolysis experiments with the 19-tosylates of the 19-hydroxy-$\Delta^{4,6}$- and $\Delta^{4,7}$-3-ketones (**8b**) and **8c**) are described as alternate approaches to (**4b**) and (**4c**). Exposure of 5β.19-cyclo compounds (**4b**) and (**4c**) to acetic anhydride-acetic acid-*p*-toluenesulfonic acid yields the respective 3-acetoxycycloheptatrienes (**5a**) and (**6a**). The latter substance (**6a**) is converted into the novel tetracyclic 1,6-methano-[10]annulene (**2a**) on exposure to N-bromosuccinimide in boiling carbon tetrachloride. Synthesis of the corresponding 3-methoxy- and 3-desoxy-1,6-methano-[10]annulenes (**2b**) and (**2c**) are also described. The NMR spectra of (**2a**), (**2b**) and (**2c**) and related intermediates are discussed.

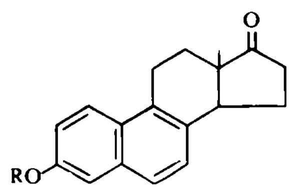
The 1,6-bridged cyclodecapentaenes depicted by expression **1** represent an interesting class of non-benzenoid aromatic hydrocarbons. Annulenes **1a–c** contain a 10π electron system and, in accord with Huckel's rule, these substances exhibit many of the physical and chemical properties of classical aromatic compounds.[1] Thus annulenes **1a–c** exhibit a diamagnetic ring current, an established criterion of aromaticity, the olefinic proton resonances for **1a–c** occurring at δ 6·8–7·3 ppm in the NMR.[1a] The 1,6-methano-[10]annulene (**1a**) undergoes substitution reactions when treated with various electrophilic reagents, as expected for an aromatic system.[1a] The close relationship of annulene **1a** to the classical aromatic substance naphthalene prompted us to undertake the synthesis of a new series of polycyclic naphthalene-type compounds in which the aromatic portion is replaced by the 1,6-methano-[10]annulene system.



1a X = CH_2
b X = CF_2
c X = O



2a R = CH_3CO_2; R_1 = O
b R = MeO; R_1 = O
c R = H; R_1 = 17β-OAc, 17α-H



3a R = H
b R = Me

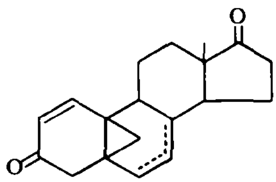
* Contribution #390 from Syntex Institute of Organic Chemistry. Part of this work was reported by J. A. Edwards at the Third International Congress on Hormonal Steroids at Hamburg, Germany, September 7–12 (1970).

† Syntex Postdoctoral Fellow (a) 1967–1968.

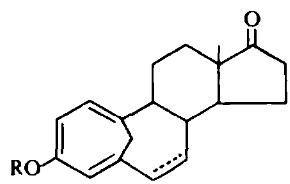
‡ Syntex Postdoctoral Fellow (b) 1968–1969.

As an initial entry into the annulene field, we selected for synthesis the tetracyclic systems **2a–c** which are the 1,6-methano-[10]annulene analogs of the substance equilenin (**3a**), a naturally occurring steroidal estrogen.

The γ,δ-cyclopropyl-α,β-unsaturated ketones (**4b,c**), bearing an additional double bond in the B ring, were selected as initial synthetic goals. Previous work from these laboratories demonstrated that the cycloheptatrienes (**5c, d**) are readily formed from the γ,δ-cyclopropyl-α,β-unsaturated ketone (**4a**) on treatment with Ac_2O and methyl orthoformate, respectively, in the presence of an acid catalyst.[2] Hence the intermediates (**4b, c**) were expected to undergo ring expansion to yield the dihydro



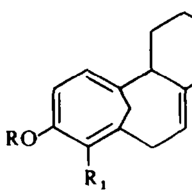
4a ring B sat'd
b with 6,7-double bond
c with 7,8-double bond



5a R = CH_3CO; with 6,7-double bond
b R = Me; with 6,7-double bond
c R = CH_3CO; ring B sat'd
d R = Me; ring B sat'd
e R = Me; with 6,7-double bond and 17,17-dimethyl ketal

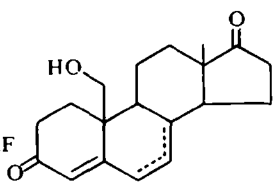
annulenes (**5a, b**) and (**6a, b**) under the same conditions. Conversion of these cycloheptatrienes into the requisite 10π electron systems (**2a, b**) could then be accomplished by a suitable dehydrogenation procedure.

Entry into the 5β,19-cyclo-$\Delta^{1,6}$-3-keto system was initially achieved following the method of Knox *et al.*,[2] who showed that reaction of 19-hydroxyandrost-4-ene-3,17-dione (**8a**) with diethyl-(2-chloro-1,1,2-trifluoroethyl)-amine[3] (**7**) (fluoramine) in

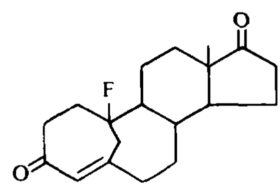


6a R = CH_3CO; R_1 = H
b R = Me; R_1 = H
c R = CH_3CO; R_1 = Br
d R = Me; R_1 = H; with 17,17-dimethyl ketal

$(Et)_2NCF_2CHClF$
7



8a ring B sat'd
b with 6,7-double bond
c with 7,8-double bond



9

boiling MeCN gives the 5β,19-cyclo-Δ^1-3-ketone (**4a**) in 47% yield, in addition to 38% yield of the bridged fluoro enone (**9**). When the 19-hydroxy-$\Delta^{4,6}$-3-ketone (**8b**)[4] was allowed to react with the fluoramine (**7**) under the same conditions, the desired 5β,19-cyclo-$\Delta^{1,6}$-3-ketone (**4b**) was isolated in only 9% yield from a complex mixture of products after extensive chromatographic purification. Substance **4b** was identified by elemental analysis and spectroscopic data (Table 1 and Experimental). The major

TABLE 1. NMR SPECTRAL DATA

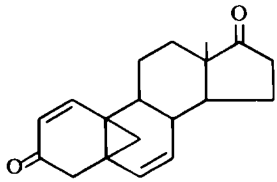
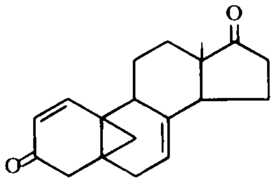
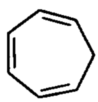
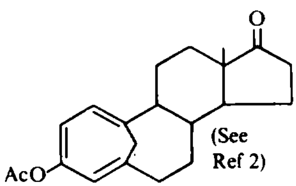
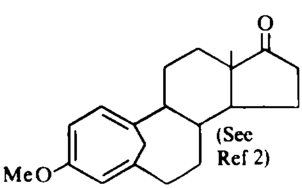
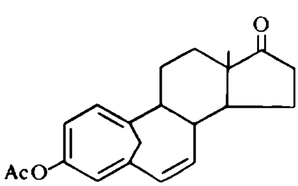
Compound	$\delta_{H_{18}}$ (ppm)	$\delta_{H_{19}}$ (ppm)	$J_{H_{19}-H_{19}}$ (Hz)	$J_{C^{13}-H_{19}}$ (Hz)	δ olefinic H's
 **4b**	0·95	0·54 d 1·78 d	4·5	165	7·55 d (J = 10·0) H_1 5·88 d (J = 10·0) H_2 5·89 dd (J = 10·0, 3·0) H_6 5·54 dd (J = 10·0, 1·5) H_7
 **4c**	0·73	0·45 d 1·22 d	4·0	168	7·24 bd (J = 10·0) H_1 coupled to H_{19} 5·77 d (J = 10·0) H_2 5·20 m H_7
 (See Ref 14)		1·43 (−170°) 2·89 (−170°)		130 J_{C_7-H}	5·28 $H_{1,6}$ 6·12 $H_{2,5}$ 6·55 $H_{3,4}$
 **5c**	1·03	1·17 d 3·33 d	10·0		5·85–6·47
 **5d**	1·02	1·08 d 3·13 d	10·0		5·7–6·3
 **5a**	1·02	0·43 d 3·54 d	9·0		6·39 d (J = 7·0) H_1 6·20 bd (J = 7·0) H_2 6·15 dm (J = 11·0) H_6 5·98 bs H_4 5·36 dd (J = 11·0, 3·0) H_7

TABLE 1—*continued*

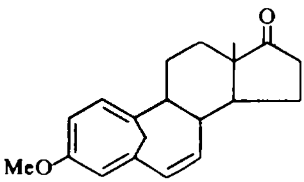
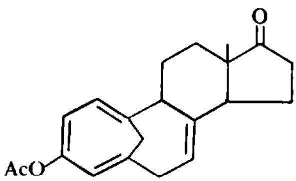
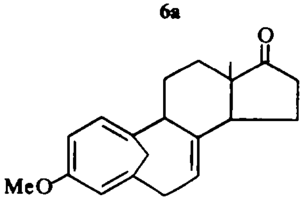
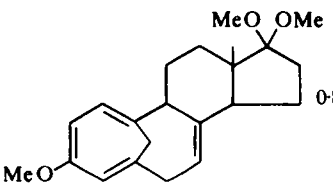
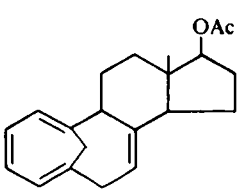
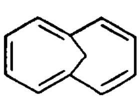
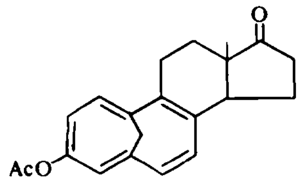
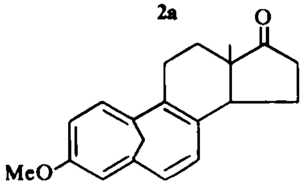
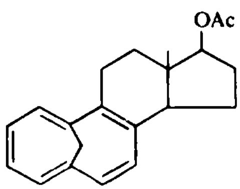
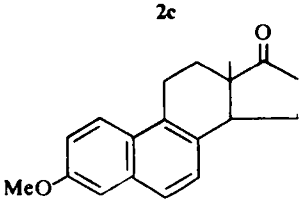
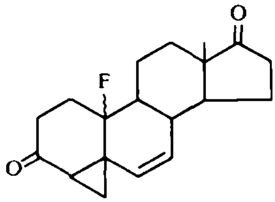
Compound	$\delta_{H_{18}}$ (ppm)	$\delta_{H_{19}}$ (ppm)	$J_{H_{19}-H_{19}}$ (Hz)	$J_{C13-H_{19}}$ (Hz)	δ olefinic H's
 **5b**	0·99	0·25 d 2·93 d	7·0		6·1 m (3H) $H_{1,2,6}$ 5·50 nm H_4 5·35 dd (J = 10·0, 2·0) H_7
 **6a**	0·83	0·76 d 2·75 d	8·0	145	6·29 d (J = 6) H_1 6·18 bd (J = 6) H_2 5·84 nm H_4 5·14 m H_7
 **6b**	0·81	0·58 d 2·34 d	7·0		6·06 d (J = 8·0) H_1 5·95 dd (J = 8·0, 1·5) H_2 5·50 bd (J = 1·5) H_4 5·15 m H_7
 **6d**	0·81	0·41 d 2·23 d	6·5	145 ± 2	6·09 d (J = 8·0) H_1 5·94 dd (J = 8·0, 2) H_2 5·45 bd (J = 2) H_4 5·05 m H_7
 **23c**	0·83	0·18 d 2·33 d	6·5	150 ± 3	6·47 m $H_{2,3}$ 6·09 m $H_{1,4}$ 5·06 m H_7
 (See Ref 1) **1a**		−0·2		142	6·8 —7·5

TABLE 1—*continued*

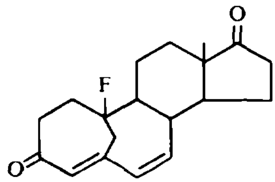
Compound	$\delta_{H_{18}}$ (ppm)	$\delta_{H_{19}}$ (ppm)	$J_{H_{19}-H_{19}}$ (Hz)	$J_{C13-H_{19}}$ (Hz)	δ olefinic H's
 2a	0·97*	−0·20 d −0·41 d	9·0		7·48 d (J = 10) H_6 7·24 d (J = 10) H_1 7·10 m H_4 6·96 d (J = 10) H_2 6·78 d (J = 10) H_7
 2b	0·95	−0·47 d −0·31 d	9·0		7·46 d (J = 10·0) H_6 7·25 d (J = 9·5) H_1 6·97 d (J = 10) H_7 6·88 m H_4 6·84 bd (J = 9·5) H_2
 2c	0·98	−0·20 d −0·61 d	9·0		6·8–7·6
 3b	0·77				7·83 bd (J = 10·0) H_6 7·60 bd (J = 8·0) H_1 7·2 m $H_{2,4,7}$

* Spectrum measured in CCl_4

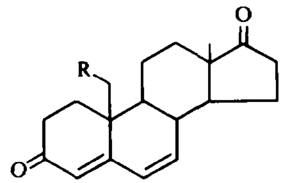
product of this reaction, isolated in 23% yield, was a fluorine containing substance which is assigned structure **10** on the basis of the following evidence. The NMR spectrum of **10** showed a multiplet at 1·2–1·35 ppm attributable to cyclopropyl protons and two pairs of doublets centered at 4·99 and 5·88 ppm for the 6 and 7-olefinic protons. Resonance ascribable to a proton in the environment H—C—F was absent. Hence the carbon atom bearing the fluorine must be tetrasubstituted. The product showed no UV absorption attributable to a conjugated carbonyl chromophore, whereas the IR spectrum showed a band at 1680 cm^{-1} in agreement with an α-cyclopropyl ketone. Treatment of **10** in boiling EtOH containing HCl



10

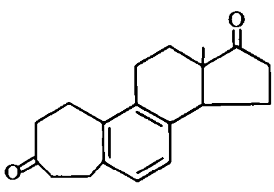


11

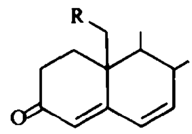


12a R = $HFClCCO_2$
b R = Cl

resulted in opening of the cyclopropane ring with concomitant loss of hydrogen fluoride to give in 68% yield the A-homo-3-ketone (**13**) which contains an aromatic B ring. The aromatic protons of **13** appear as an AB quartet with doublets at 7·00 and 7·09 ppm, $J_{6,7}$ 6·5 Hz. Three other products were isolated from this fluoramine reaction and identified by their elemental analysis and spectroscopic properties as the bridged 10β-fluoro enone (**11**; *ca.* 8%), the 19-chlorofluoroacetate (**12a**; 4%), and the 19-chloro-$\Delta^{4,6}$-3-ketone (**12b**; 13%). The latter product was also identified by comparison with an authentic sample. Formation of **12a** and **12b** can be rationalized from the intermediate iminium salt (**14**). Thus reaction of the latter species with water gives rise to the chlorofluoroacetate (**12a**),[2,5] whereas attack of chloride ion at C-19 of the salt yields the 19-chloro compound (**12b**) and N,N-diethyl chlorofluoroacetamide.*



13



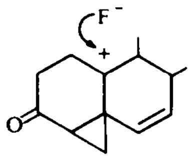
14

R = $-O-C(CHFCl)=\overset{+}{N}(C_2H_5)_2$

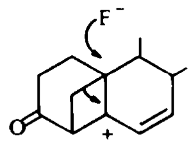
The other products can be depicted as arising by the intervention of fluoride ion with the isomeric cationic species (**a**, **b**, **c**) which are derivable from **14** by loss of N,N-diethyl chlorofluoroacetamide. Presumably stabilization of the positive charge in **b** by the 6,7-double bond promotes buildup of the 4β,5β-methylene product. Proton abstraction from C-1 by fluoride ion (species **d**) also competes to a certain extent with the fluoride ion substitution processes and leads to the 5β,19-cyclo-$\Delta^{1,6}$-3-ketone (**4b**).[2]

On account of the poor yield of 5β,19-cyclo-$\Delta^{1,6}$-3-ketone (**4b**) obtained in the fluoramine reaction, we next considered solvolysis experiments with the 19-tosyloxy-$\Delta^{4,6}$-3-ketone (**15**) as a possible route to **4b**. In principle, solvolysis of tosylate (**15**) in the presence of a suitable base could proceed by proton abstraction from C-1 *via*

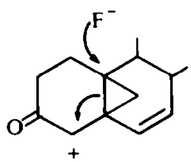
* Although the source of chloride ion responsible for the formation of **12b** has not been established, it is known that chloride ion competes favourably with fluoride ion in the reaction of certain steroid alcohols with the fluoramine. See ref. 6.



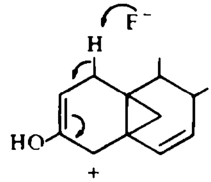
a



b

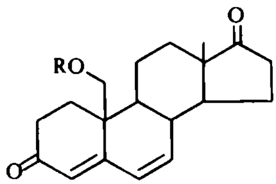


c



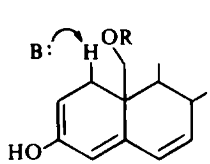
d

the enol (**16**) followed by rearrangement of the carbanion (**17**) (arrows) with the departure of tosylate to form a new carbon-carbon bond between C-5 and C-19.*† Accordingly, a solution of the 19-tosylate (**15**) in DMF containing lithium carbonate was heated under reflux until starting material disappeared. Purification of the



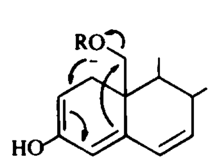
15

R = $CH_3C_6H_4SO_2$



16

R = $CH_3C_6H_4SO_2$



17

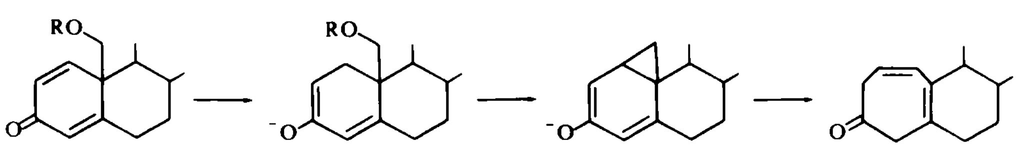
R = $CH_3C_6H_4SO_2$

resulting crude product by chromatography over silica gel gave the desired 5β,19-cyclo-$\Delta^{1,6}$-3-ketone (**4b**) in 24% yield as the only isolatable product. Tosylate (**15**) was recovered unchanged after being refluxed in pyridine for 8 hr. With boiling collidine or heating in pyridine at 150° in a sealed tube, **15** was slowly transformed into **4b**, but a number of other products were also formed. Heating the tosylate (**15**) with anhyd KF in DMSO at 120° gave in 40% yield the unsaturated ketocyclobutane (**18**). This substance showed a UV max at 235 nm (ε 13,800) and olefinic proton resonance at 5·60 (singlet) and 5·92 ppm (broadened doublet, $J_{6,7}$ 7 Hz) ascribable to the 4-H and 7-H respectively. The 6-H appeared as a doublet of doublets centered at 3·41 ppm ($J_{6,7}$ 7 Hz, $J_{6,19}$ 5 Hz).

The reaction of 19-hydroxyandrosta-4,7-diene-3,17-dione (**8c**)[9] with fluoramine (**7**) proceeded much more clearly than in the case of the 19-hydroxy-$\Delta^{4,6}$-3-ketone (**8b**) to afford in 46% yield the desired 5β,19-cycloandrosta-4,7-diene-3,17-dione (**4c**) as the only identifiable product apart from N,N-diethyl chlorofluoroacetamide. The

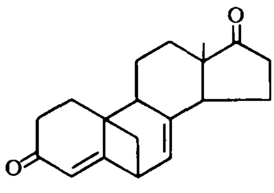
* The hydrolysis of 19-sulfonyloxy-Δ^4-3-ketones to the 6β,19-cycloenones has been described. See ref. 7.

† It is interesting to note that generation of a carbanion at C-1 by reduction of (i) with lithium and biphenyl affords the A-homodienone (iv) *via* the intermediate 1β,19-cyclo species (iii). See ref. 18.

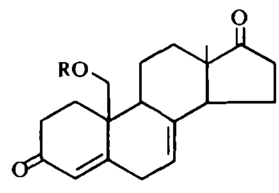


i R = CH_3SO_2 ii R = CH_3SO_2 iii iv analytical and spectral properties of **4c** were in accord with the assigned structure. The outcome of the latter reaction further emphasizes the contribution of the 6,7-double bond in altering the course of the fluoramine reaction with the 19-hydroxy-$\Delta^{4,6}$-3-ketone (**4b**) as compared with the 19-hydroxy-$\Delta^{4,7}$-3-ketone (**8c**) and 19-hydroxyandrost-4-ene-3,17-dione.[2]

Before proceeding with the ring opening experiments with **4b** and **4c**, the solvolysis of the 19-tosyloxy-$\Delta^{4,7}$-3-ketone (**19**) was investigated. Since tosylate (**19**) was obtained as an amorphous solid which tended to decompose on attempted purification, the solvolysis experiments were carried out on crude **19**. Thus stirring tosylate **19** in benzene solution in the presence of alumina (activity I) gave in 40% yield 6β,19-cycloandrosta-4,7-diene-3,17-dione (**18**) which was obtained previously by



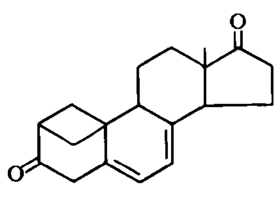
18



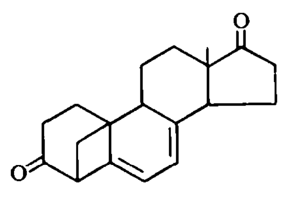
19

R = $CH_3C_6H_4SO_2$

reaction of the 19-tosyloxy-$\Delta^{4,6}$-3-ketone (**15**) in DMSO containing KF. Heating tosylate **19** in boiling pyridine solution for 2 hr furnished a mixture of two products which was separable by chromatography over alumina. The more polar substance (16%) was identical to the 6β,19-cyclo-$\Delta^{4,7}$-3-ketone (**18**) obtained from the alumina reaction. The less polar compound (33%) was an isomer of **18**, and since the substance showed resonance in the olefinic proton region attributable to only two vicinal protons, it must possess either the 2β,19-cyclo structure (**20**) or the 4β,19-cyclo structure (**21**). The presence of an AB pattern at 3·06 and 3·50 ppm, J_{gem} 15·5 Hz in



20

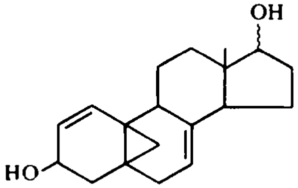


21

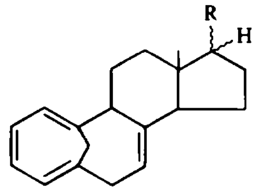
the NMR spectrum of this product is consistent with a methylene group in the environment O═C—CH_2—C═C and thereby defines the structure as **20**.

Both the Δ^6- and Δ^7-enones (**4b** and **4c**) were cleanly transformed into their respective 3-acetoxycycloheptatrienes (**5a** and **6a**) on treatment at room temp with AcOH–Ac_2O mixture containing *p*-TsOH acid.[2] Similarly, exposure of **4b** and **4c** to methyl orthoformate and an acid catalyst in MeOH gave the 3-methoxycycloheptatrienes (**5b** and **6b**) respectively, together with their corresponding 17,17-dimethyl ketals (**5c** and **6d**).

The 3-desoxycycloheptatriene (**23c**) was prepared by reducing the 5β,19-cyclo-$\Delta^{1,7}$-3-ketone (**4c**) to a mixture of $\Delta^{1,7}$-3β,17-diols (**22**)* epimeric at C-17 by the Meerwein–Ponndorf technique[10] followed by treatment with *p*-TsOH in boiling benzene. Chromatography of the resulting product furnished the 17α- and 17β-hydroxycycloheptatrienes (**23a** and **23b**) as amorphous solids, the latter alcohol being characterized as a crystalline acetate (**23c**).



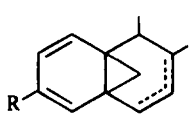
22



23a R = 17α-OH, 17β-H
b R = 17β-OH, 17α-H
c R = 17β-OAc, 17α-H

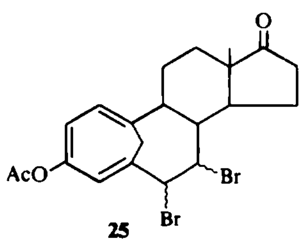
The cycloheptatriene structures are favored for substances **5a**, **b** and **6a**, **b** rather than the norcaradiene system (e.g., **24**) on the basis of the H—H and ^{13}C—H coupling constants of the methylene bridge protons. These data are summarized in Table 1. Thus, the *geminal* coupling constants for **5a–d** and **6a**, **b**, **d** fall in the range 6·5–10 Hz. Published J_{gem} values for norcaradiene derivatives are in the range 3–5 Hz, whereas the J_{gem} values reported for the cycloheptatriene system are 7–12 Hz.[11] The ^{13}C—H coupling constants for the bridged protons in **6a** and **6d** are compatible with the cycloheptatriene structures since Vogel has reported $J_{^{13}C-H} = 142$ Hz for the bridged protons of 1,6-methano-[10]annulene (**1a**).[1a] Allocation of the cycloheptatriene structure to the 3-desoxy compound (**23c**) appears to be less secure as judged by the foregoing NMR parameters since the H—H and ^{13}C—H coupling constants are at the outer limits observed for the cycloheptatriene system. There was, however, no change in J_{gem} from $-60°$ to $+80°$.

For the conversion of 3-acetoxy-5,10-*seco*-5,19-cycloandrosta-1(10),2,4,6-tetraen-17-one (**5a**) to the desired annulene (**2a**), dehydrogenation experiments utilizing Pd/C, 2,3-dichloro-5,6-dicyanobenzoquinone,† SeO_2, MnO_2, $Pb(OAc)_4$ and $Cr(CO)_6$

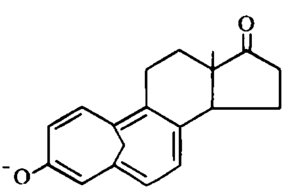


24

R = H, MeO, CH_3CO_2



25



26

* The reduction of **4c** by various metal hydride reagents (LAH, $NaBH_4$, Li(t-BuO)$_3$AlH) proceeded by 1,4-addition of hydride to yield the 5β,19-cyclo-3-ketone or the corresponding 3-alcohol when $NaBH_4$ was employed.

† This reagent has been used for the synthesis of 1,6-methano-[10]annulene. See ref. 12.

were uniformly unsuccessful. More promising results were obtained by treating **5a** with N-bromosuccinimide in boiling CCl_4 under illumination with a 150 watt lamp. Purification of the product by chromatography over silica gel afforded 13% of the crystalline 6ξ,7ξ-dibromide (**25**) and 34% of an annulene fraction which was repurified by prep. TLC. The strongly UV fluorescing zone was eluted to yield a solid (75% purity) containing the desired annulene (**2a**) as the major component as judged by NMR spectroscopy. Exposure of dibromo compound **25** to boiling xylene containing 3 molar equiv of s-collidine followed by prep. TLC also afforded impure annulene (**2a**) in 11% yield. Attempts to obtain analytically pure **2a** by repeated prep TLC and/or recrystallization failed.

Pure acetoxyannulene (**2a**) was finally obtained by allowing 3-acetoxy-5,10-seco-5,19-cycloandrosta-1(10),2,4,7-tetraen-17-one (**6a**) to react with N-bromosuccinimide in boiling CCl_4 containing lithium carbonate, the reaction being initiated by irradiation with a 200 watt lamp. Purification of the resulting product by chromatography over silica gel impregnated with $AgNO_3$ gave the desired acetoxyannulene (**2a**) in 15·5% yield as a nicely crystalline solid, m.p. 159–160·5°, together with a small amount of the 3-acetoxy-4-bromo compound (**6c**). The NMR spectrum of pure **2a** showed the bridge methylene protons as an AB quartet with doublets at −0·41 and −0·20 ppm and the aromatic protons as a multiplet at 7·10 ppm for the 4-H which appears between two AB quartets of the vicinal aromatic protons (Table 1). The NMR spectrum of 1,6-methano-[10]annulene shows the bridge methylene protons as a singlet at −0·50 ppm and the aromatic protons as an A_2B_2 system centered at 7·10 ppm.[1a]

Acetoxyannulene (**2a**) was also obtained in 20% yield by heating (**6a**) in *t*-butyl perbenzoate and a catalytic amount of CuCl at 95–100° followed by purification by alumina chromatography. Similar treatment of the 3-desoxy-Δ^7-cycloheptatriene (**23c**) with *t*-butyl perbenzoate gave in 27% yield the desired annulene (**2c**) as an amorphous solid whose NMR (Table 1) and mass spectral data were in agreement with the assigned structure. However, the ε value observed for the UV spectrum of **2c** is substantially lower than the corresponding values observed for the UV spectra of **2a**, **b**, indicating that **2c** is probably not an analytically pure substance.

All attempts to convert the Δ^6- and Δ^7-3-methoxycycloheptatrienes (**5b** and **6b**) into the 3-methoxyannulene (**2b**) by the foregoing procedures were unsuccessful. The latter substance was obtained by treating acetoxyannulene (**2a**) with methanolic KOH containing dimethyl sulfate, the intermediate enolate (**26**) initially formed being methylated to **2b** under the reaction conditions. The desired **2b** was obtained as a crystalline solid, m.p. 162°, in 51% yield.

NMR *spectroscopy*. The 19-protons of 5β,19-cycloandrostane-3,17-dione resonate at 0·43 and 0·57 ppm.[13] In **4a** the presence of the 1,2-double bond causes a 0·61 ppm downfield shift of Ha, the proton *syn* to the A ring, relative to Ha in the saturated analog.[2] In the case of the 5β,19-cyclo-$\Delta^{1,6}$-3,17-diketone (**4b**) (Table 1) the 6,7-double bond causes further deshielding of Ha (0·60 ppm) as well as Hb (0·07 ppm) relative to the respective protons in the NMR spectrum of **4a** through conjugation of the second carbon–carbon double bond with the cyclopropane ring. However, Hb is somewhat shielded by the anisotropy of the 6,7-double bond and thus does not undergo the same downfield shift as observed for Ha. The Hb resonance of the 5β,19-cyclo-$\Delta^{1,7}$-3,17-diketone (**4c**) appears at 0·45 ppm. A larger upfield shift might be expected for this signal owing to the shielding effect of the 7,8-double bond. However, examination of Dreiding models of **4a**, **b**, **c** reveals that with **4c** Hb is closer to the C-18 angular Me group than is Hb of **4a** and **4b**. Accordingly, Hb of substance **4c** experiences additional deshielding as a result of increased steric compression between Hb and the 18-protons. This effect partially reduces the strong shielding by the 7,8-double bond present in **4c**. The *geminal* and ^{13}C—H coupling constants for the 19-H in **4b** and **4c** demonstrate the presence of the cyclopropane system in these compounds.

In cycloheptatriene compounds it has been demonstrated that the methylene proton resonance at higher field is due to the proton *syn* to the triene system.[2,14] Examination of Dreiding models reveals that in **5a** and **5b** Ha is closer to the 2,3-double bond than is Ha of **5c** and **5d**. As expected the Ha resonance in **5a** and **5b** is shifted upfield by *ca* 0·7 ppm relative to Ha resonances of the ring B saturated cycloheptatrienes **5c** and **5d**. Similar although smaller upfield shifts (0·4–0·5 ppm) of Ha are also observed in the Δ^7-compounds (**6a** and **6b**). In the latter compound Hb is also strongly shielded (0·6–0·8 ppm) due to the anisotropy of the 7,8-double bond. Shifting of the double bond from the 6,7-position, e.g., **4b**, **5a** or **5b** to the 7,8-position, e.g., **4c**, **6a** or **6b** is accompanied by a 0·2 ppm upfield shift of the 18-protons. Since a 0·12 ppm upfield shift is predicted from the values of Zürcher,[15] the observed chemical shifts indicate stronger shielding of the 18-H by the 7,8-double bond than is observed for steroids lacking the 5β,19-cyclo system. Interestingly this additional shielding must be sufficiently large to overcome the deshielding effects resulting from steric compression between Hb and the C-18 angular Me group.

The annulene derivatives (**2a**, **b**, **c**) exhibited NMR spectral properties reminiscent of 1,6-methano-[10]annulene (**1a**).[1a] The higher field shifts of the 19-protons compared to the bridge protons of **1a** are presumably due to the increased shielding of the steroid nucleus. The olefinic proton resonances for **2a**, **b**, **c** are at somewhat higher field than the olefinic proton resonances observed for equilenin 3-methyl ether (**3b**) and indicate a loss of aromatic character and a reduced ring current due to nonplanarity of the annulene system. These effects are quite comparable to those observed by Vogel for **1a**. The downfield shift of the 18-H in **2a**, **b**, **c** relative to that observed for **3** is also compatible with the reduced effectiveness of the shielding ring current as well as deshielding arising from steric compression between the methylene bridge and the 18-protons.

EXPERIMENTAL*†

Reaction of 19-*hydroxyandrosta*-4,6-*diene*-3,17-*dione* (**8b**) *with the fluoramine* (**7**). A solution of 19-hydroxyandrosta-4,6-diene-3,17-dione (**8b**) (2 g) and fluoramine (**7**) (1·5 ml) in MeCN (30 ml, distilled from P_2O_5) was heated under reflux in a N_2 atmosphere for one hr. The red-brown solution was evaporated *in vacuo* and the resulting syrup dissolved in 30 ml of C_6H_6–CH_2Cl_2 (1:1) and adsorbed on a column of

* M.ps are uncorrected. Optical rotations were measured in $CHCl_3$ soln at 27° and UV spectra in 95% EtOH unless specified otherwise. NMR spectra were recorded for 5–10% solution (w/v) in $CDCl_3$ containing TMS as internal reference on Varian A-60 and HA-100 spectrometers. Chemical shifts are reported as ppm on the δ scale. Mass spectra were obtained with an Atlaswerke CH-4 spectrometer equipped with a direct inlet system. Spectra were measured at an ionizing potential of 70 eV and an acceleration voltage of 3 KV. Microanalyses were performed by A. Bernhardt, Mulheim (Ruhr), West Germany.

† Preparative TLC was conducted using silica gels GF and HF (from Brinkmann Instruments Inc., N.Y) at thicknesses of 1·3 mm and steroid loadings of 2 mg/cm.

silica gel (80 g). The column was washed with 800 ml of CH_2Cl_2–EtOAc (9:1) and 500 ml of pure EtOAc. Evaporation of the latter fraction yielded 0·6 g of resinous solid which was discarded. Evaporation of the first eluate, followed by trituration of the resulting solid with cold MeOH gave 4β,5β-methylene-10ξ-fluoroestr-6-ene-3,17-dione (**10**) (0·46 g, 23%), m.p. 228–229°; ν_{max} 1735, 1680 cm^{-1}; NMR 0·95 (s, 18-H), 1·2–1·35 (m, cyclopropyl-H), 4·99 (d of d, J = 9·5, 2·7 Hz, 6 or 7-H), 5·88 ppm (d of d, J = 9·5, 2·0 Hz, 6 or 7-H). (Found: C, 75·56; H, 7·87. $C_{19}H_{23}O_2F$ requires C, 75·46; H, 7·66%).

Purification of the mother liquors by prep TLC using hexane–ether (3:7—two developments) yielded. in order of decreasing polarity: (a) 19-chlorofluoracetoxyandrosta-4,6-diene-3,17-dione (**12a**) (81 mg, 4%) amorphous; $[\alpha]_D$ +123° (dioxane); λ_{max} 278 nm (ε 19,800); NMR 0·98 (s, 18-H), 4·44, 4·52 (AB portion of ABX system, J_{AB} = 12·0 Hz, J_{AX} 2·0 Hz, J_{BX} = 4·0 Hz, 19-H), 5·89 (s, 4-H), 6·06, 6·57 (d, J_{HF} = 51·0 Hz, —CHFCl), 6·25 ppm (s, 6, 7-H). (Mass spectrum 394 (M^+) $C_{21}H_{24}O_4FCl$ requires: MW 394·9). (b) 19-chloroandrosta-4,6-diene-3,17-dione (**12b**) (0·26 g, 13%), m.p. 165–166° (from EtOH); $[\alpha]_D$ +115° (dioxane); λ_{max} 281 nm (ε 21,100); NMR 1·00 (s, 18-H), 3·66, 3·86 (AB quartet, J_{AB} = 12·5 Hz, 19-H), 5·79 (s, 4-H), 6·22 ppm (s, 6, 7-H). (Found: C, 71·88; H, 7·42. $C_{19}H_{23}O_2Cl$ requires: C, 71·50; H, 7·27%). (c) 10β-fluoro-5,10-seco-5,19-cycloandrosta-4,6-diene-3,17-dione (**11**) (11% admixed with **4b** and isolated in pure state by chromatography over alumina), m.p. 200–202° (from MeOH); $[\alpha]_D$ +271° (dioxane); λ_{max} 281 nm (ε 16,200); NMR 0·95 (s, 18-H), 5·75 (broad s, 4-H), 5·96 (d of d, $J_{6,7}$ = 11·5 Hz, $J_{6 \text{ or } 7,8}$ = 2·1 Hz, 6 or 7-H), 6·54 ppm (broadened d, $J_{6,7}$ = 11·5 Hz, 6 or 7-H). (Found: C, 76·01; H, 7·68. $C_{19}H_{23}O_2F$ requires: C, 75·56; H, 7·66%). (d) 5β,19-cycloandrosta-1,6-diene-3,17-dione (**4b**) (0·17 g, 8%), m.p. 195–196° (from EtOAc); λ_{max} 245, 290 (sh) nm (ε 5340, 2750); NMR see Table 1. (Found: C, 80·77; H, 7·86; O, 11·56. $C_{19}H_{22}O_2$ requires: C, 80·81; H, 7·85; O, 11·33%).

19-*Chloroandrosta*-4,6-*diene*-3,17-*dione* (**12b**). A solution of 19-hydroxyandrosta-4,6-diene-3,17-dione (**8b**) (0·3 g) in DMF (9 ml) was treated with triphenylphosphine (0·38 g) and CCl_4 (0·48 ml).* The mixture was heated on the steam bath for 15 min, cooled, diluted with water and the resulting solution extracted with EtOAc. The organic extracts were washed with water, dilute $NaHCO_3$aq and water, dried (Na_2SO_4) and evaporated. A solution of the residue in benzene was filtered through a column of alumina (12 g) and evaporated. Crystallization of the resulting solid from EtOH gave **12b**, m.p. 165–166° identical in all respects with a sample obtained from the fluoramine reaction with **8b**.

A-Homo-estra-5,7,9-*triene*-3,17-*dione* (**13**). A solution of the fluoro compound (**10**) (0·16 g) dissolved in EtOH (6·3 ml) containing conc HCl (1·6 ml) was heated under reflux for 1 hr. The solvents were evaporated *in vacuo* and the residue was dissolved in CH_2Cl_2 and adsorbed on a column of silica gel (10 g). Elution with 100 ml of ether–hexane (3:7) gave 0·1 g of **13**, m.p. 151° (from MeOH); $[\alpha]_D$ +86° (diox); λ_{max} 223 (sh), 268, 278 nm (ε 12,800, 630, 520); NMR 0·76 (s, 18-H), 2·4–2·7 (m, 6-protons, 2, 4, 16-H), 2·8–3·1 (m, 7-protons, 1, 4a, 9, 14-H), 7·00, 7·09 ppm (ABq, J_{AB} = 6·5 Hz, 6, 7-H). (Found: C, 80·95; H, 8·17. $C_{19}H_{22}O_2$ requires: C, 80·81; H, 7·85%).

19-*Tosyloxyandrosta*-4,6-*diene*-3,17-*dione* (**15**). A solution of 19-hydroxyandrosta-4,6-diene-3,17-dione (**8b**) (10 g) and *p*-TsCl (12 5 g) in dry pyridine (150 ml) was kept for 20 hr at 0° and 5 hr at 20 . The mixture was poured into water and the precipitate collected, washed well with water, dried and crystallized from EtOH to yield the tosylate (**15**) (14 1 g, 92%), m.p. 164–165°; $[\alpha]_D$ +110° (dioxane); λ_{max} 223, 278 nm (ε 14,800, 18,800). (Found: C, 68·85; H, 6·96; O, 17·72. $C_{26}H_{30}O_5S$ requires: C, 68·69; H, 6·65; O, 17·60%).

Solvolysis of 19-*tosyloxyandrosta*-4,6-*diene*-3,17-*dione* (**15**) *in dimethylformamide*. Lithium carbonate (20 g) was added to a solution of 19-tosylate (**15**) (5 g) in dry redistilled DMF (250 ml) and the resulting mixture was heated under reflux with stirring in a N_2 atmosphere for 12 hr. The experiment was repeated with another 5 g of **15** and the combined mixtures were filtered through celite and evaporated under reduced pressure to a volume of 100 ml. Water was added and the aqueous mixture was extracted with 3 × 250 ml portions of EtOAc. The organic extracts were washed with water, dilute $NaHCO_3$aq and water, dried (Na_2SO_4) and evaporated. The resulting solid was dissolved in ether–hexane (2:3) and filtered through a column of silica gel (350 g). Evaporation of the eluates gave 5β,19-cycloandrosta-1,6-diene-3,17-dione (**4b**) (1·45 g, 24%), m.p. 191–192°, identical in all respects with a sample of **4b** obtained from the fluoramine reaction with **8b**.

Solvolysis of 19-*tosyloxyandrosta*-4,6-*diene*-3,17-*dione* (**15**) *in dimethyl sulfoxide*. A solution of the tosylate (**15**) (0·5 g) in DMSO (20 ml) was stirred with anhyd. KF (1 g) at 120° for 4 hr in a N_2 atmosphere. The

* We thank Drs B. Berkoz, J. P. Verheyden and J. G. Moffatt for providing these unpublished experimental conditions.

mixture was cooled, diluted with water and extracted with 2 × 50 ml of EtOAc. The EtOAc solution was washed with water, dried ($MgSO_4$) and evaporated to yield a gum which was purified by prep TLC over silica gel using ether–hexane (9:1). This yielded 0·13 g of 6β,19-cycloandrosta-4,7-diene-3,17-dione (**18**) (40%), m.p. 140–141° (acetone–hexane); $[\alpha]_D$ +154° (dioxane); λ_{max} 235 nm (ε 13,800): NMR 0·84 (s, 18-H), 3·41 (pair of d, $J_{6,7}$ 7·0 Hz, $J_{6,19}$ = 4·5 Hz, 6-H), 5·60 (s, 4-H), 5·92 ppm (broadened d, $J_{6,7}$ = 7 Hz, 7-H). (Found: C, 80·79; H, 7·92; O, 11·54. $C_{19}H_{22}O_2$ requires: C, 80·81; H, 7·85; O, 11·33%).

Reaction of 19-hydroxyandrosta-4,7-diene-3,17-dione (**8c**) *with the fluoramine* (**7**). 19-Hydroxyandrosta-4,7-diene-3,17-dione (**8c**) (7·4 g) was dissolved in warm dry MeCN (250 ml, distilled from P_2O_5) and the fluoramine (**7**) (6 ml) was added. The solution was heated under reflux for 1 hr, cooled and partitioned between ether and water. The aqueous phase was extracted twice with ether and the combined organic extracts were washed once with 5% $NaHCO_3$aq, twice with water, dried (Na_2SO_4) and evaporated to afford a brown oil which was purified by chromatography on alumina (400 g, activity III). Elution with hexane gave the liquid diethylchlorofluoroacetamide. Continued elution with hexane–benzene (1:3) gave essentially pure 5β,19-cycloandrosta-1,7-diene (**4c**) (3·2 g, 46%), m.p. 182–183°; $[\alpha]_D$ +187°; λ_{max} 265 nm (ε 5200); NMR see Table 1. (Found: C, 80·75; H, 7·62. $C_{19}H_{22}O_2$ requires: C, 80·81; H, 7·85%).

19-Tosyloxyandrosta-4,7-diene-3,17-dione (**19**). Solutions of 19-hydroxyandrosta-4,7-diene-3,17-dione (**8c**) (2·6 g) in pyridine (8 ml) and *p*-TsCl (2·6 g) in pyridine (2 ml) were mixed and stirred at room temp for 66 hr. The mixture was processed exactly as described for **15** to yield tosylate **19** as a labile gum, ν_{max}^{film} 1740, 1675, 1635, 1600, 1480, 1175 cm^{-1}.

Solvolysis of 19-tosyloxyandrosta-4,7-diene-3,17-dione (**19**) *in pyridine*. Half of the foregoing crude tosylate (**19**) was dissolved in pyridine (15 ml) and the resulting solution heated under reflux for 2 hr, cooled and diluted with benzene. This solution was washed with an excess of 5% HCl aq. The acid washings were back-extracted with two portions of benzene and the combined benzene extracts washed with water, dried (Na_2SO_4) and evaporated. This afforded a gum which was dissolved in hexane and chromatographed on 80 g of alumina (activity III). Elution with hexane–benzene (1:3) and pure benzene afforded 0·4 g (33%) of 2β,19-cyclo steroid (**20**) as a gum which crystallized on trituration with ether–hexane, m.p. 97–98°; $[\alpha]_D$ +30°; λ_{max} 270 nm (ε 3800); ν_{max} 1735, 1700, 1605 cm^{-1}; NMR 0·71 (s, 18-H), 1·13, 2·89 (AB q, J_{AB} = 10·0 Hz, cyclobutyl-H), 3·06, 3·50 (AB q, J_{AB} = 16·0 Hz, 4-H), 6·01, 6·35 ppm (pair of d, $J_{6,7}$ = 5·5 Hz, 6, 7-H). (Found: C, 81·00; H, 8·04. $C_{19}H_{22}O_2$ requires: C, 80·81; H, 7·85%). Continued elution with ether gave 6β,19-cycloandrosta-4,7-diene-3,17-dione (**18**) (0·19 g, 15·5%), m.p. 140–141°, identical in all respects with a sample of **18** obtained from the solvolysis of tosylate (**15**) in DMSO.

Treatment of 19-tosyloxyandrosta-4,7-diene-3,17-dione (**19**) *with alumina*. The remaining crude tosylate (**19**) was dissolved in benzene (50 ml) and stirred with 20 g of alumina (activity I) for 5 hr. The alumina was filtered, washed with ether and the combined filtrates evaporated to yield a gum. This was purified by chromatography over 50 g of alumina (activity III), to furnish 6β,19-cyclo steroid (**18**) (0·48 g, 39·5%), m.p. 138–140°, identical with a sample obtained from the preceding experiment.

3-Acetoxy-5,10-seco-5,19-cycloandrosta-1(10),2,4,6-tetraen-17-one (**5a**). A solution of 5β,19-cycloandrosta-1,6-diene-3,17-dione (**4b**) (0·8 g) in 12·5 ml of dry AcOH–Ac_2O (4:1) containing *p*-TsOH (50 mg) was kept for 1 hr at 20° in N_2 atmosphere. Pyridine (1 ml) was added, the solution poured into water, and the solid collected by filtration. Crystallization of the resulting solid from MeOH furnished **5a** (0·81 g, 89%), m.p. 188–189°; $[\alpha]_D$ +376° (dioxane); λ_{max} 236, 287 nm (ε 20,660, 5130); NMR see Table 1. (Found: C, 77·58; H, 7·48. $C_{21}H_{24}O_3$ requires: C, 77·75; H, 7·46%).

3-Acetoxy-5,10-seco-5,19-cycloandrosta-1(10),2,4,7-tetraen-17-one (**6a**). A solution of 5β,19-cycloandrosta-1,7-diene-3,17-dione (**4c**) (0·51 g) in AcOH (20 ml) containing Ac_2O (2 ml) and *p*-TsOH (0·31 g) was kept for 3 hr at 20° and then processed as described in the preceding experiment. This gave **6a** (0·49 g, 84·5%), m.p. 154–155° (from MeOH + a drop of pyridine); $[\alpha]_D$ +313°; λ_{max} 257 nm (ε 4160); NMR see Table 1. (Found: C, 77·97; H, 7·21. $C_{21}H_{24}O_3$ requires: C, 77·75; H, 7·46%).

3-Methoxy-5,10-seco-5,19-cycloandrosta-1(10),2,4,6-tetraen-17-one (**5b**). A solution of 5β,19-cyclo-androsta-1,6-diene-3,17-dione (**4b**) (0·52 g) in dioxane (7 ml) containing MeOH (1·7 ml), methyl orthoformate (3·5 ml) and *p*-TsOH (35 mg) was allowed to stand for 1 hr at room temperature and then treated with 20 drops of pyridine. Water was added and the resulting solution extracted with several portions of EtOAc. The combined extracts were washed with water, dilute $NaHCO_3$ and water, dried (Na_2SO_4) and evaporated. The residue was crystallized from MeOH containing a trace of pyridine to give the 17,17-dimethyl ketal (**5e**) (0·32 g, 50%), m.p. 164–165°; $[\alpha]_D$ +266° (dioxane); λ_{max} 239, 288 nm (ε 12,370, 2870). (Found: C, 77·18; H, 8·84; O, 13·96. $C_{22}H_{32}O_3$ requires: C, 76·78; H, 9·13; O, 13·93%). Purification of the mother liquors by prep TLC (hexane–ether, 2:1) furnished the 17-ketone (**5b**) (81 mg, 15%), m.p. 174–176°

(from MeOH + a drop of pyridine); $[\alpha]_D$ +403° (dioxane); λ_{max} 240, 286 nm (ε 17,314, 4240); NMR see Table 1. (Found: C, 81·21; H, 8·26. $C_{20}H_{24}O_2$ requires: C, 81·04; H, 8·16%).

3-*Methoxy*-5,10-*seco*-5,19-*cycloandrosta*-1(10),2,4,7-*tetraen*-17-*one* (**6b**). A solution of 5β,19-cycloandrosta-1,7-diene-3,17-dione (**4c**) (0·48 g) in MeOH containing methyl orthoformate (0·4 ml) and oxalic acid (30 mg) was heated under reflux for 30 min. The cooled solution was diluted with ether, washed with dilute $NaHCO_3$ and water, dried (Na_2SO_4) and evaporated. The residue was adsorbed from hexane onto 50 g of *alumina* (activity III). Elution with hexane afforded 0·15 g of dimethyl ketal (**6d**) (26%), m.p. 113–114°; $[\alpha]_D$ +181°; λ_{max} 246 nm (ε 3150); NMR see Table 1. (Found: C, 76·83; H, 8·89. $C_{22}H_{30}O_3$ requires: C, 77·15; H, 8·83%). Continued elution with hexane–benzene (4:1) afforded 0·25 g of 17-ketone (**6b**) (49%), m.p. 110–112°; $[\alpha]_D$ +290°; λ_{max} 247 nm (ε 3420); NMR see Table 1. (Found: C, 80·89; H, 7·80. $C_{20}H_{24}O_2$ requires: C, 81·04; H, 8·16%).

5,10-*Seco*-5,19-*cycloandrosta*-1(10),2,4,7-*tetraen*-17β-*ol acetate* (**23c**). A solution of 5β,19-cycloandrosta-1,7-diene-3,17-dione (**4c**) (0·51 g) in dry i-PrOH (25 ml) containing redistilled aluminum isopropoxide (1 g) was slowly distilled over 3 hr, *ca.* 5 ml of distillate being collected. The cooled solution was poured into ice water (250 ml) containing 1N HCl acid (18 ml) and the resulting mixture was kept at 0 until the precipitate coagulated. The solid was collected and dried to yield 0·49 g of diol mixture (**22**) as a white powder. This mixture (172 mg) was dissolved in benzene (15 ml) and stirred with *p*-TsOH (35 mg) for 20 min. The solution was washed with 5% $NaHCO_3$aq and water, dried (Na_2SO_4) and evaporated to yield a yellow gum as a mixture of 17-alcohols. This was purified by prep TLC using ether/hexane (1:1) to afford 5,10-seco-5,19-cycloandrosta-1(10),2,4,7-tetraen-17β-ol (**23b**) (68 mg) as an oil, NMR 0·19, 2·35 (AB q, J_{AB} = 6·5 Hz, 19-H), 0·68 (s, 18-H), 3·80 (t, 17α-H), 5·01 (m, 7-H), 6·05 (m, 2, 3-H), 6·34 ppm (q, 1, 4-H) and the corresponding 17α-ol (**23a**) (26 mg) as an oil, NMR 0·20, 2·37 (AB, q, J_{AB} = 7·0 Hz, 19-H), 0·61 (s, 18-H), 3·85 (d, J = 6·0 Hz, 17β-H), 5·09 (m, 7-H), 6·09 (m, 2, 3H), 6·39 ppm (m, 1, 4-H). Acetylation of **23b** (68 mg) by treatment (18 hr) with pyridine (3 ml) containing Ac_2O (10 drops) produced the crystalline acetate (**23c**) (66 mg), m.p. 98–99° (from MeOH); $[\alpha]_D$ +127·5°; λ_{max} 260 nm (ε 3260); NMR see Table 1. (Mass spectrum 310 (M^+). $C_{21}H_{26}O_2$ requires: MW 310·4).

Attempted preparation of 3-*acetoxy*-5,10-*seco*-5,19-*cycloandrosta*-1(10),2,4,6,8-*pentaen*-17-*one* (**2a**) *from* 3-*acetoxy*-5,10-*seco*-5,19-*cycloandrosta*-1(10),2,4,6-*tetraen*-17-*one* (**5a**). A solution of **5a** (0·38 g) in CCl_4 (17 ml) containing N-bromosuccinimide (0·25 g) was heated under reflux, the mixture being irradiated with a 150 watt tungsten lamp. After 15 min, 43 mg of N-bromosuccinimide was added and the mixture was heated for another 15 min. The red-brown solution was cooled, filtered and the filtrate immediately washed with $NaHCO_3$aq and water, dried (Na_2SO_4) and evaporated. The residue was dissolved in hexane and adsorbed on a column of silica gel (50 g). Elution with hexane and hexane–EtOAc (9:1) gave 6ξ,7ξ-dibromide (**25**) (75 mg, 13%), m.p. 184–186° (from MeOH–trace pyridine); $[\alpha]_D$ +268° (dioxane); λ_{max} 212, 254 (sh), 295–300 (sh) nm (ε 21,800, 8540, 2200); NMR 0·95, 3·58 (AB q, J_{AB} = 11·5 Hz, 19-H) 1·07 (s, 18-H), 2·20 (s, 3-acetoxy-H), 4·47, 4·94 (two d, $J_{6,7'}$ = 3 Hz, 6, 7-H), 6·03 (s, 4-H), 6·16 (d, $J_{1,2}$ = 6 Hz, 2-H), 6·60 ppm (d, $J_{1,2}$ = 6 Hz, 1-H) (mass spectrum 482, 484, 486 (M^+); $C_{21}H_{24}Br_2O_3$ requires: MW 484·2) and an annulene fraction (0·13 g). The latter material was further purified by prep TLC on silica gel using hexane–EtOAc (9:1). This gave 28 mg of solid (75% pure by TLC and VPC analysis), shown to be mainly the annulene (**2a**) by NMR, −0·47 to −0·15 (ill resolved AB, q J_{AB} = 9·0 Hz, 19-H), 0·99 (s, 18-H), 2·31 (s, 3-acetoxy-H), 6·8–7·6 ppm (m, consisting of 2 AB q and 1 s, aromatic-H).

3-*Acetoxy*-5,10-*seco*-5,19-*cycloandrosta*-1(10),2,4,6,8-*pentaen*-17-*one* (**2a**). A. N-bromosuccinimide method. N-Bromosuccinimide (89 mg) and lithium carbonate (50 mg) were added to a solution of dihydroannulene (**6a**) (0·138 g) in CCl_4 (15 ml) and the resulting mixture was heated under reflux for 45 min, the reaction being initiated by irradiation with a 200 watt lamp. The cooled solution was washed with water, dried (Na_2SO_4) and evaporated. This reaction was repeated using 0·18 g and 0·4 g of **6a** and the crude products were combined with the first experiment, dissolved in ether–hexane (1:1) and filtered through a column of silica gel (20 g) to remove polar impurities. The resulting solid obtained after removal of the solvent was purified by prep TLC using silica gel GF impregnated with $AgNO_3$ and ether–hexane (1:1). Two major product zones were eluted from the plates in addition to recovered starting material (89 mg). The fraction less polar than starting (**6a**) weighed 45 mg and was purified further by filtration through a column of silica gel (4 g) in ether–hexane (1:4). This yielded 16·8 mg of bromo compound (**6c**), m.p. 186–187° (dec) (from MeOH); $[\alpha]_D$ +214°; λ_{max} 275 nm (ε 3900); NMR 0·81 (s, 18-H), 1·03, 2·64 (AB q, J_{AB} = 8·5 Hz, 19-H), 2·22 (s, 3-acetoxy-H), 5·13 (m, 7-H), 6·04, 6·27 ppm (AB, q J_{AB} = 7·0 Hz, 1, 2-H). (Found: C, 62·71; H, 5·68. $C_{21}H_{23}O_3Br$ requires: C, 62·53; H, 5·75%).

The strongly fluorescing zone more polar than starting **6a** was essentially pure acetoxyannulene (**2a**)

(0·11 g, 15·5%), m.p. 159–160·5°; $[\alpha]_D$ +248°; λ_{max} 265, 309 nm (ε 50,900, 5800); NMR (CCl_4) see Table 1. (Found: C, 77·56; H, 7·00. $C_{21}H_{22}O_3 \cdot \frac{1}{4}H_2O$ requires: C, 77·20; H, 6·94%). (Mass spectrum 322 (M^+); $C_{21}H_{22}O_3$ requires: MW 322·4).

B. *t*-Butyl perbenzoate method. Dihydroannulene (**6a**) (0·44 g) and a trace of CuCl were heated with stirring in t-butyl perbenzoate (2·5 ml) under N_2 at 95–100°. The yellow solution became first green and then deep red. After 2 hr the cooled solution was diluted with hexane and applied to a column of alumina (45 g, activity III). Elution with hexane yielded t-butyl perbenzoate. Elution with hexane–ether (8:1) afforded 0·12 g of crystalline annulene (**2a**) (27%), identical by TLC and NMR comparisons with a sample of **2a** obtained from preceding reaction.

5,10-Seco-5,19-cycloandrosta-1(10),2,4,6,8-pentaen-17β-ol acetate (**2c**). Dihydroannulene (**23c**) (0·17 g) and a trace of CuCl were heated under reflux in a 1% solution of t-butyl perbenzoate in benzene (10 ml) for 12 hr. The solution was evaporated to dryness and the residue chromatographed on 7 g of alumina (activity III). Hexane eluted unchanged reagent and hexane–benzene (4:1) eluted 65 mg of gum: TLC of latter material showed the presence of starting **23c** and the major product as a highly fluorescent spot. Further purification by prep TLC on silica plates (hexane–ether, 2:1) gave **2c** (54 mg, 32%) as an oil homogeneous by TLC: $[\alpha]_D$ −25°; λ_{max} 263 nm (ε 34,500); NMR see Table 1. (Mass spectrum 308 (M^+); $C_{21}H_{24}O_2$ requires: MW 308·4).

3-Methoxy-5,10-seco-5,19-cycloandrosta-1(10),2,4,6,8-pentaen-17-one (**2b**). Acetoxyannulene (**2a**) (0·18 g) was dissolved in MeOH and treated with 2 drops of dimethyl sulfate and 6 drops of 1 N methanolic KOH. After 5, 10 and 15 min intervals, an additional drop of dimethyl sulfate was added. The solution was kept alkaline by dropwise addition of methanolic alkali. After 20 min the mixture was partitioned between ether and water and the organic phase separated, washed with $NaHCO_3$aq and water, dried (Na_2SO_4) and evaporated. The resulting dark gum was dissolved in hexane and adsorbed on a column of alumina (activity III). Elution with hexane–benzene (4:1) yielded 0·1 g of crystalline annulene (**2b**) (61%), m.p. 162° (from MeOH); $[\alpha]_D$ +333°; λ_{max} 268, 309 nm (ε 44,400, 6085); NMR see Table 1. (Mass spectrum 294 (M^+); $C_{20}H_{22}O_2$ requires: MW 294·4).

Acknowledgments—We thank Dr John Fried for his interest and encouragement. We also thank Drs P. Nelson and K. G. Untch for helpful discussions on the NMR aspects of this work. We thank Mrs P. Nelson for the NMR determinations and Dr L. Tökés and Mr J. Smith for the mass spectra.

REFERENCES

[1] [a] See E. Vogel, *Aromaticity*, Special Publication No. 21, The Chemical Society, pp. 113–147 (1967); [b] V. Rautenstrauch, H.-J. Scholl and E. Vogel, *Angew. Chem. Int. Ed. Engl.* 7, 288 (1968); E. Vogel and H. Günther, *Ibid.* 7, 385 (1968); A. Shani and F. Sondheimer, *J. Am. Chem. Soc.* **89**, 63 (1967)

[2] L. H. Knox, E. Velarde and A. D. Cross, *J. Am. Chem. Soc.* **87**, 3727 (1965)

[3] N. N. Yarovenko and M. A. Raksha, *Zh. Obshck. Khim.* **29**, 2159 (1959); *Chem. Abstr.* **54**, 9724h (1960)

[4] K. Heusler, J. Kalvoda, C. Meystre, H. Ueberwasser, P. Wieland, G. Anner and A. Wettstein, *Experientia* **18**, 464 (1962)

[5] L. H. Knox, E. Velarde, S. Berger, D. Cuadriello and A. D. Cross, *J. Org. Chem.* **29**, 2187 (1964)

[6] E. J. Bailey, E. Fazakerly, M. E. Hill, C. E. Newall, G. H. Phillips, L. Stephenson and A. Tulley, *J. Chem. Soc.* D, 106 (1970)

[7] J. J. Bonet, H. Wehrli and K. Schaffner, *Helv. Chim. Acta* **45**, 2615 (1962); O. Halpern, P. Crabbé, A. D. Cross, I. Delfin, L. Cervantes and A. Bowers, *Steroids* **4**, 1 (1964)

[8] P. Wieland and G. Anner, *Helv. Chim. Acta* **51**, 1932 (1968)

[9] J. F. Bagli, P. F. Morand, K. Wiesner and R. Gaudry, *Tetrahedron Letters* 387 (1964)

[10] For examples see D. N. Kirk and A. Mudd, *J. Chem. Soc.* C, 804 (1969)

[11] G. Maier, *Angew. Chem. Int. Ed. Engl.* **6**, 402 (1967)

[12] P. H. Nelson and K. G. Untch, *Tetrahedron Letters* 4475 (1969)

[13] J. J. Bonet, H. Wehrli and K. Schaffner, *Helv. Chim. Acta* **45**, 2615 (1962)

[14] F. A. L. Anet, *J. Am. Chem. Soc.* **86**, 458 (1964); F. R. Jensen and L. A. Smith, *Ibid.* **86**, 956 (1964)

[15] R. F. Zürcher, *Helv. Chim. Acta* **46**, 2054 (1963)