Tetrahedron, 1967, Vol. 23, pp. 1515 to 1534. Pergamon Press Ltd. Printed in Northern Ireland

MODIFIED STEROID HORMONES—XLVII[1]

SOME FURTHER PENTACYCLIC TYPES

J. M. ALLISON, D. BURN, F. K. BUTCHER, M. T. DAVIES and V. PETROW
Chemical Research Department, The British Drug Houses Ltd., Graham Street, London

(*Received* 11 *July* 1966)

Abstract—A route to pentacyclic steroid derivatives has been developed involving the condensation of steroidal 16-hydroxymethylene-17-ketones with methyl vinyl ketone. The stereochemistry of the products has been investigated.

THE anti-inflammatory activity of the steroidal cortical hormones may be enhanced by alkyl substitution at certain positions of the molecule, eg. at C-16.[2] Anti-inflammatory activity is not confined however, to the steroids, and is possessed[3] to some degree by, for example, the pentacyclic triterpene glycerrhetic acid.[4] We therefore prepared some novel pentacyclic steroids in which C-16 and C-17 form part of a carbocyclic ring. While this work was in progress some related studies by other investigators appeared in the literature.[5]

Pentacyclic steroids in which an additional six-membered ring is built onto Ring A of the steroid skeleton may be prepared[6] by condensing a 2-hydroxymethylene-3-ketone with methyl vinyl ketone and cyclising the resulting 2-(3'-oxobutyl)-3-ketone.[7] An analogous synthetic pathway has now been employed for the preparation of steroidal derivatives having an additional 6-membered ring attached to Ring D. Reaction of the model compound 16-hydroxymethylene-3β-hydroxyandrost-5-en-17-one with methyl vinyl ketone in pyridine containing triethylamine gave a product which yielded on chromatographic separation three substances conveniently designated *A*, *B* and *C*.

Substance *A*, $C_{28}H_{34}O_3$, the major component, has been assigned the structure 3β-hydroxy-16α-(3'-oxobutyl)androst-5-en-17-one (I)* on the following evidence. The

* The stereochemistry at C_{16} is discussed in detail later in this paper.

[1] Part XLVI, C. Burgess, D. Burn, P. Feather, M. Howarth and V. Petrow, *Tetrahedron* **22**, 2829 (1966).

[2] See, for example, G. E. Arth, J. Fried, D. B. R. Johnson, D. R. Hoff, L. H. Sarett, R. H. Silber, H. C. Stoerk and C. A. Winter, *J. Amer. Chem. Soc.* **80**, 3161 (1958); E. P. Oliveto, R. Rausser, A. L. Nussbaum, W. Gebert, E. B. Hershberg, S. Tolksdorf, M. Eisler, P. L. Perlman and M. M. Pechet, *Ibid.* p. 4428; E. P. Oliveto, R. Rausser, L. Weber, A. L. Nussbaum, W. Gebert, C. T. Coniglio, E. B. Hershberg, S. Tolksdorf, M. Eisler, P. L. Perlman and M. M. Pechet, *Ibid.* p. 4431; E. P. Oliveto, R. Rausser, H. L. Herzog, E. B. Hershberg, S. Tolksdorf, M. Eisler, P. L. Perlman and M. M. Pechet, *Ibid.* p. 6687.

[3] See, for example, S. D. Kraus, *J. Pharm. Pharmac.* **12**, 300 (1960).

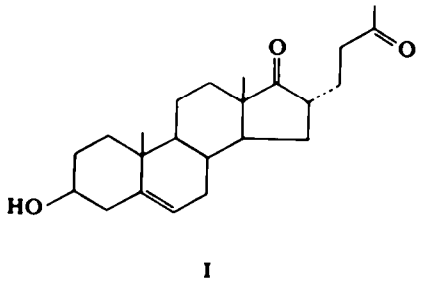
[4] J. M. Beaton and F. S. Spring, *J. Chem. Soc.* 3126 (1955) and Refs. there cited.

[5] See, for example, M. E. Wall, S. Serota, H. E. Kenney and G. S. Abernethy *J. Amer. Chem. Soc.* **85**, 1844 (1963); P. Bladon and T. Sleigh, *J. Chem. Soc.* 3264 (1962); S. G. Levine, M. E. Wall and N. H. Eudy, *J. Org. Chem.* **28**, 1936 (1963); J. E. Pike, M. A. Rebenstorf, G. Slomp and F. A. Mackellar, *J. Org. Chem.* **28**, 2499, 2502 (1963).

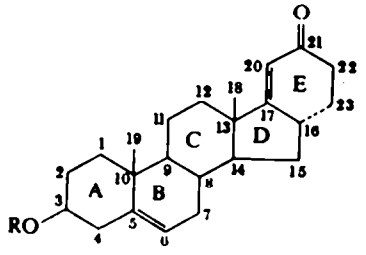
[6] G. Cooley, J. W. Ducker, B. Ellis, V. Petrow and W. P. Scott, *J. Chem. Soc.* 4108 (1961).

[7] Y. Urushibara and J. Inomata, *Bull. Chem. Soc. Japan* **32**, 101 (1959).

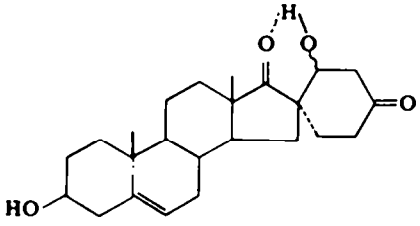
IR spectrum revealed the presence of the 17-ketone (band at 1730 cm^{-1}) and one other saturated ketone (band at 1708 cm^{-1}). A band in the NMR spectrum at ca. 7·85 τ established the presence of a methyl ketone, whilst both the NMR and IR spectra indicated the absence of a formyl group. Treatment of the 16α-(3'-oxobutyl)-17-ketone (I) with hot aqueous alcoholic alkali effected cyclisation and gave a compound, $C_{23}H_{32}O_2$, formulated as 3β-hydroxypentara-5,17(20)-dien-21-one* (II; R = H). The presence of the αβ-unsaturated carbonyl group was established by UV absorption at 237 mμ and by IR absorption at 1678 and 1647 cm^{-1}. The cyclisation product formed a mono-acetate (II; R — Ac), lacking hydroxyl absorption in the IR.



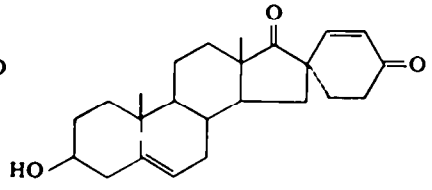
I



II



III



IV

The two minor components *B* and *C*, obtained by chromatography of the reaction product have been assigned the spirocyclic structures III and IV on the basis of the following evidence. Substance *B*, $C_{24}H_{34}O_4$, contains at least one hydroxyl group (3593 and 3494 cm^{-1}) and two carbonyl groups. These carbonyl groups give rise to one broad band† (1709 cm^{-1} in Nujol, 1720 cm^{-1} in CH_2Cl_2), the area of which corresponds to two groups. Presumably hydrogen bonding (see III) shifts the 17-ketone absorption to longer wavelength, very close to that of the 4'-ketone. In addition, the NMR spectrum indicated the absence of formyl and $CO{\cdot}CH_3$ groups. On treatment of the compound with acetic anhydride-pyridine, acetylation with concomitant dehydration occurred to give a substance $C_{26}H_{34}O_4$ which proved to be identical with the acetate prepared from the minor component C. The latter compound retains the 17-ketone moiety (1733 cm^{-1}) and, in addition to one acetate group, contains an αβ-unsaturated ketone (1680 and 1610 cm^{-1}). The anomalous

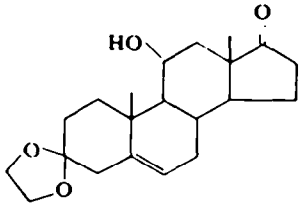
* Note on nomenclature. In order to avoid the cumbersome 16,17-cyclohex-2'-en-4'-one nomenclature, it is proposed to assign the trivial name 'pentarane' to the carbon skeleton exemplified by structure (II) and to adopt the numbering shown. The stereochemistry of the D/E ring junction is specified by the configuration of the hydrogen atoms at C_{16} and C_{17}.

† In one case (Experimental), the carbonyl groups give rise to a doublet in Nujol.

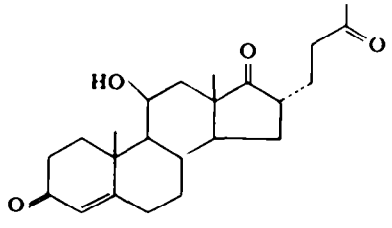
UV spectrum, namely the presence of 3 maxima (see experimental), could possibly result from charge transfer between the 17-ketone and $\alpha\beta$-unsaturated ketone, which from models are favourably orientated for asymmetric orbital overlap to occur.[8] The formation of compounds III and IV is explained by assuming that the initial condensation product is a 16-formyl-16-oxobutyl-17-ketone. During chromatography on alkaline alumina, this intermediate is transformed into products III and IV by separate reaction pathways involving (i) elimination of the formyl group by a reverse Claisen condensation and (ii) cyclisation, not involving the C-17-ketone, by an aldol condensation. The amounts of compounds III and IV isolated however, reveal that the latter reaction occurs only to a minor extent. Partial dehydration of compound III on alkaline alumina is not unexpected.

The preparative route exemplified by the transformations 16-hydroxymethylene-17-ketone → (I) → (II) has been applied to a wide variety of steroidal starting materials, preferably without purification of the crude condensation products, when the overall yields of pentacyclic derivatives were generally in the order of 35–45%. The facile condensation of steroidal 3-ketones with ethyl orthoformate (at C-2) precluded their use as starting materials in this synthetic route. 3-Ketals and 3-hydroxy starting materials were quite suitable, and the pentacyclic products were readily converted into the required 3-ketones.

Pentranes oxygenated at C-11 are of especial interest from the standpoint of anti-inflammatory activity. Suitable starting materials for their preparation were readily obtained from cortisone.* Thus, vigorous borohydride reduction of cortisone acetate 3-ketal and its 5α-dihydro analogue, followed by periodate cleavage of the resulting 11β,17α,20,21-tetrols, gave the 17-ketones V (Δ^5 and 5α H). An alternative procedure was employed to prepare 11β-hydroxy-5β-pentar-17(20)-ene-3,21-dione. The 16-3′-oxobutyl derivative obtained from 3,3-ethylenedioxy-11β-hydroxyandrost-5-en-17-one was deketalised to the corresponding 4-en-3-one (VI). Catalytic hydrogenation of the latter compound under alkaline conditions gave the 5β-dihydro derivative which was cyclised to the required pentarane. 5α- and 5β-dihydro-3-hydroxy pentaranes were prepared from 5α- and 5β-dihydrocortisone acetates by borohydride reduction to the 5α-dihydro-3β,11β,17α,20,21- and 5β-dihydro-3α,11β,17α,20,21- pentols, periodate cleavage to the corresponding androstan-17-ones and application of the described pentarane synthesis. In order to prepare a 9α-fluoropentarane, the 11β-hydroxy-3-ketal V (Δ^5) was dehydrated ($POCl_3$-pyridine) to the 9(11)-ene which was converted into the corresponding pentarane. Introduction of the 9α-fluoro-11β-hydroxy system



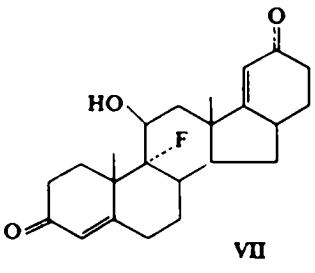
V



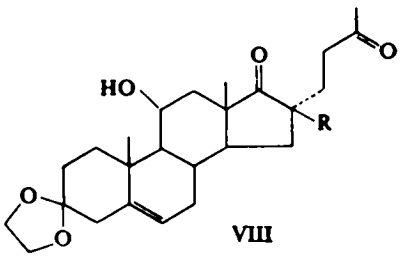
VI

* Essentially similar procedures have been described in the literature, cf. Ref. e, Table 4.

[8] R. Grinter, S. F. Mason and G. W. Vane, *Trans. Faraday Soc.* 60, 285 (1964) and references there cited.



VII

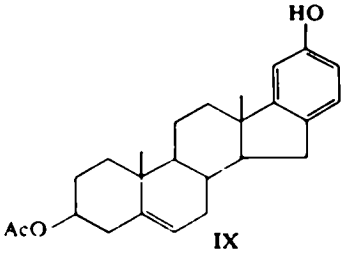


VIII

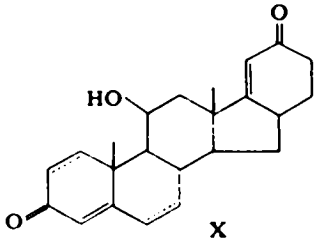
into the derived 4-en-3-one followed standard practice[9] and afforded the required 9α-fluoro-11β-hydroxypentara-4,17(20)-diene-3,21-dione (VII).

The earlier speculations regarding the probable source of the spirocyclic by-products obtained from reaction between 16-hydroxymethylene-17-ketones and methyl vinyl ketones were convincingly established by the isolation of condensation products which retain the C-16 formyl group. Thus the condensation (Experimental) between 3,3-ethylenedioxy-11β-hydroxy-16-hydroxymethyleneandrost-5-en-17-one and methyl vinyl ketone yielded a product which did not require chromatography for purification. The analytical and spectroscopic data presented in the experimental section support the structure VIII (R = CHO) assigned to this compound. In addition, treatment of this 16-formyl-16-3′-oxobutyl-17-ketone with alkali under mild conditions, (or passage through an alumina column), afforded mainly the corresponding 16-desformyl derivative VIII (R = H) together with a smaller amount of the spirocyclic αβ-unsaturated ketone, whilst under more drastic conditions, the corresponding pentarane was obtained.

With a view to preparing 1,4-dien- and 4,6-dien-3-one derivatives in the 11β-hydroxypentarane series, the reaction of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)[10] and of chloranil[11] with 3β-acetoxypentara-5,17(20)-dien-21-one (II; R = Ac) was investigated. Both reagents produced the same product which is formulated as the phenol IX as it forms a methyl ether and a diacetate. The IR of the latter compound revealed the presence of both aliphatic (1739 and 1240 cm^{-1}) and aromatic (1768 and 1208 cm^{-1}) acetates. The NMR spectrum of IX exhibited the characteristic aromatic AB system (ca. 3 τ). The required 1,4-dien- X (Δ^1) and 4,6-dien-3-ones X (Δ^6) were ultimately prepared by DDQ and chloranil dehydrogenations respectively of 11β-hydroxy-16-3′-oxobutylandrost-4-ene-3,17-dione (VI), followed by base-catalysed cyclization to the pentaranes.



IX



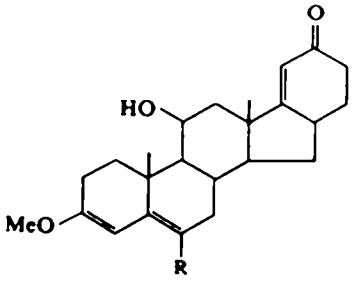
X

[9] See for example, J. Fried and E. F. Sabo, *J. Amer. Chem. Soc.* **76**, 1455 (1954); R. F. Hirschmann R. Miller, J. Wood and R. E. Jones, *Ibid.* **78**, 4956 (1956).

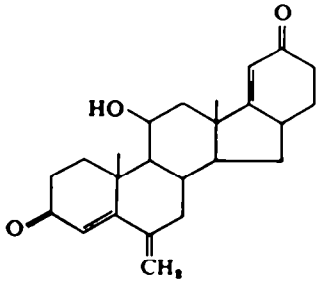
[10] D. Burn, D. N. Kirk and V. Petrow, *Proc. Chem. Soc.* 14 (1960).

[11] E. J. Agnello and G. D. Laubach, *J. Amer. Chem. Soc.* **79**, 1257 (1957); **82**, 4293 (1960).

6-Methylated pentaranes, lacking an oxygen substituent at C-11, were readily prepared from 3β-hydroxy-6-methylandrost-5-en-17-one (see Tables). As no suitable 6-alkylated intermediates carrying an 11-oxygen substituent were available, the application of the Vilsmeier process[18] to 11-oxygenated pentaranes was examined. Brief (ca. ½ hr) treatment of 11β-hydroxypentara-4,17(20)-dien-3,21-dione with methyl orthoformate and toluene-*p*-sulphonic acid resulted in selective conversion into the 3-enol methyl ether XI (R = H). The last compound showed a band in the NMR spectrum at 6·42 τ, characteristic of a methoxyl group, with an area corresponding to only 3 protons. The observation that the 17(20)-en-21-one system present in the model compound 3β-acetoxypentara-5,17(20)-dien-21-one II (R = Ac) reacted extremely slowly with methyl orthoformate under the same conditions indicates that enol etherification occurs at C-3 and not at C-21. Brief treatment of the enol ether XI (R = H) with the Vilsmeier reagent prepared from phosphoryl chloride and dimethylformamide gave the corresponding 6-formyl derivative XI (R = CHO), characterized by UV absorption at 238 (17(20)-en-21-one) and 322 mμ (6-formyl-3-methoxy-3,5-diene). Selective reduction of the formyl group was achieved by treatment with lithium borohydride under very mild conditions. Treatment of the resulting (not purified) 6-hydroxymethyl derivative XI (R = CH_2OH) with acid gave 11β-hydroxy-6-methylenepentara-4,17(20)-diene-3,21-dione (XII), characterized by UV absorption at 240 (17(20)-en-21-one) and 265 mμ (6-methylen-4-en-3-one).



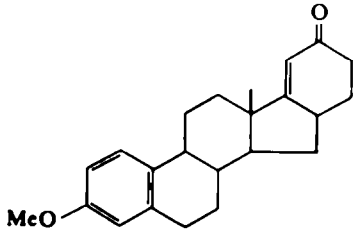
XI



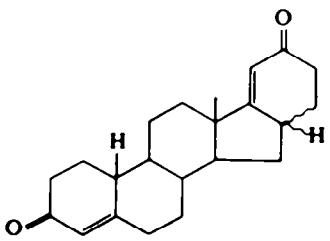
XII

We next examined the application of the foregoing synthetic routes to the preparation of 19-norpentaranes. The 16-hydroxymethylene derivative of oestrone methyl ether was submitted to the foregoing reaction sequence and afforded 3-methoxy-19-norpentara-1,3,5(10),17(20)-tetraen-21-one (XIII). Protection of the C-21-ketone as its ethylene ketal followed by Birch reduction and subsequent acid hydrolysis, gave a 19-norpentara-4,17(20)-diene-3,21-dione (XIV) having m.p. 173·5° and $[\alpha]_D$ +124°. In view of the somewhat disappointing overall yield in the above sequence, an alternative route was investigated. 3-Methoxy oestra-2,5(10)-dien-17-one was converted into the 16-hydroxymethylene derivative which was similarly submitted to the pentarane synthesis. Acid hydrolysis of the product gave a second 19-norpentara-4,17(20)-diene-3,21-dione (XIV), m.p. 179°, $[\alpha]_D$ −22·7°, differing markedly from that obtained by the first route.

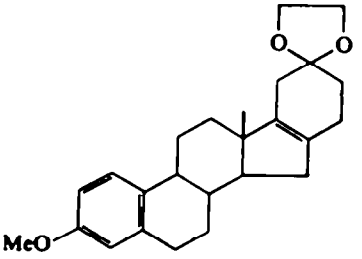
[18] D. Burn, G. Cooley, M. T. Davies, J. W. Ducker, B. Ellis, P. Feather, A. K. Hiscock, D. N. Kirk, A. P. Leftwick, V. Petrow and D. M. Williamson, *Tetrahedron* **20**, 597 (1964).



XIII



XIV



XV

The formation of two different 19-norpentaranes by these reaction sequences was totally unexpected. A possible explanation is provided by a study of the NMR spectrum of 21-ketal of XIII in which the signal due to the vinyl proton at C-20 (ca. 4·3 τ) is absent. This could indicate that the 17(20)-double bond migrates to the unconjugated 16(17)-position on ketalization of the C-21-ketone, giving XV, and moves back into conjugation upon deketalization as shown by the UV extinction coefficients of the 19-norpentaranes XIV (ε_{241} 33,000) (cf. ketalization of steroidal 4-en-3-ones). Two further pentaranes, 3β-hydroxypentara-5,17(20)-dien-21-one II (R = H) and 3β-hydroxy-5α-pentar-17(20)-en-21-one, were also converted into the corresponding 21-ketals. In each case the double-bond was shown by NMR to have migrated to the 16,17-position. On deketalization, $\alpha\beta$-unsaturated ketones were obtained which were isomeric with the original ketones. These facts indicate that the pairs of pentacyclic derivatives may be epimeric at C-16. In an attempt to elucidate their* stereochemistry, the assumption was first made that methyl vinyl ketone would attack a 16-hydroxymethylene-17-ketone from the less hindered α-side of the molecule. Thus in the 'normal' pentaranes the angular hydrogen atom at C-16 might be expected to have the β-configuration 'A', whilst in the epimeric and thermodynamically stable series, this hydrogen atom would have the 16α-configuration 'B' (Fig. 1).

The physical properties (Table 1) of the two series showed, in every respect other than ORD, only small, but consistent, differences which do not allow stereochemical assignments to be made.

Careful examination of Dreiding models of configurations A and B revealed a

* A preliminary account of this stereochemical problem was presented by Mr. M. T. Davies, The British Drug Houses Ltd. at the NATO Advanced Study Courses on ORD and CD held at Bonn in September 1965.

marked difference in the chiralities of the 17(20)-en-21-one system (Fig. 1), paralleling the difference between the 4-en-3-one system of 19-nortestosterone[14] on the one hand,

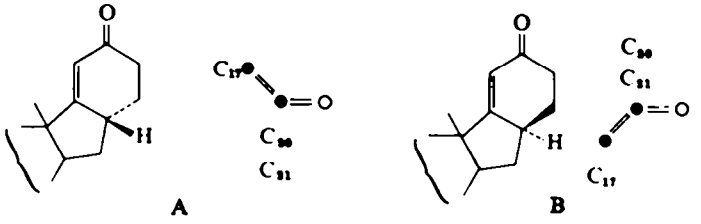


FIG. 1.

and those of both 19-nor-retrotestosterone[15] and B-norcholest-4-en-3-one[16] on the other. It has been firmly established[16] that the sign of the n–π^* transition ORD spectrum of an enone system is determined by the chirality of that system which, in

TABLE 1

—	A	B
λ_{max} (ε)	236 mμ (17,000)	242 mμ (17,000)
ν CCl_4 (21-one, 17(20)-ene)	1673, 1643 cm^{-1}	1658, 1607 cm^{-1}
*NMR (C-20-proton)	4·30 τ	4·1–4·2 τ
ORD Cotton effect	multiple, +ve	multiple, −ve

* The signal due to this proton appeared as a doublet (J 1·5 c/s) due to allylic coupling with the C-16 proton.[19]

the case of 4-en-3-ones, is controlled by the conformation (chair, or skew, induced by a *cis*-BC junction) or the size of ring B. Conformation A (Fig. 1) is associated with a multiple positive Cotton effect, while conformation B is associated with a multiple negative Cotton effect. The ORD curves obtained from dioxan solutions of the epimeric 3β-hydroxy-5α,16ξ-pentar-17(20)-en-21-ones (Fig. 2) leave little doubt that the normal and isomeric pentaranes have been correctly assigned the 16α- and 16β-configurations respectively.

We next examined the hydrogenation of the 17(20)-double bond present in representative C-16 epimeric pentaranes. In each case, the hydrogenation appeared to be essentially stereospecific. ORD data were again utilized for the determination of the stereochemistry of the resulting 17(20)-dihydro-21-ketones. Particularly noteworthy are the extremely large amplitudes (Experimental) of the Cotton effects. These amplitudes are among the largest recorded for cyclohexanones and strongly suggest twist conformations for ring E.[17] Considering first structures having a trans D/E ring junction (i.e. 16α,17β- and 16β,17α-stereochemistry), examination of corresponding Dreiding models shows that not only are the twist forms of ring E highly

[13] S. Sternhell, *Rev. Pure* and *Appl. Chem.* **14**, 15 (1964).
[14] C. Djerassi, R. Riniker and B. Riniker, *J. Amer. Chem. Soc.* **78**, 6362 (1956).
[15] P. Crabbe, *Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry* Chap. 9 and and Refs. there cited. Holden-Day, San Francisco (1965).
[16] W. B. Whalley, *Chem. & Ind.* 1024 (1962); G. Snatzke, *Tetrahedron* **21**, 413, 421 (1965).
[17] C. Djerassi and W. Klyne, *Proc. Natl. Acad. Sci.* **48**, 1093 (1962).

strained, but also that they lead to the prediction of Cotton effects of opposite signs to those observed experimentally. Of the other possible trans conformations, the boat forms lead to the prediction of Cotton effects of the wrong signs, whilst the chair

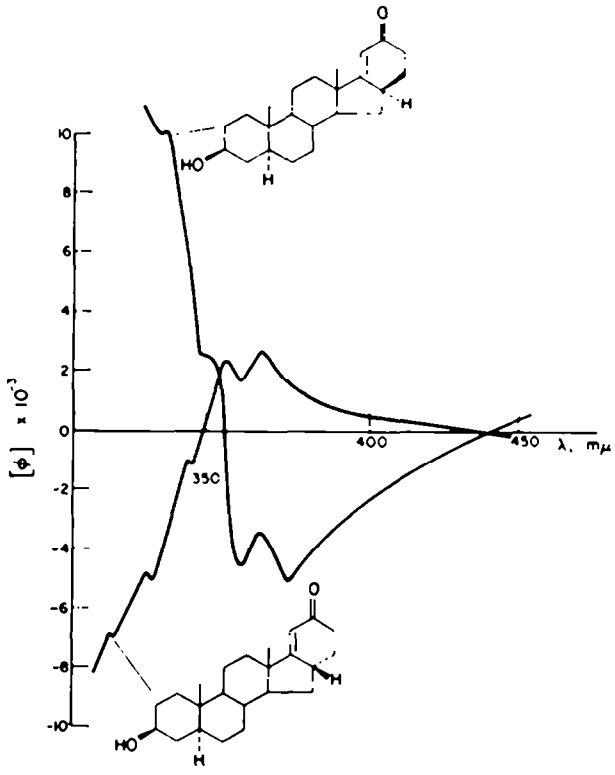


FIG. 2

forms lead to the prediction of Cotton effects of the correct signs but of considerably reduced amplitudes. Turning now to structures having a cis D/E ring junction, examination of the appropriate Dreiding models leads to the following predictions:

	16α,17α	16β,17β
Boat	+ve Cotton, small amplitude	+ve Cotton, small amplitude
Chair	−ve Cotton, small amplitude	−ve Cotton, small amplitude
Twist	−ve Cotton, large amplitude	+ve Cotton, large amplitude

The experimentally determined ORD curves of isomeric pairs of dihydropentaranes can be reconciled only with cis D/E ring junctions in which ring E is in the twist conformation. It is worth noting that Dreiding models of these *cis*-twist structures appear to be the least strained of all the possible forms.

One of the saturated pentaranes (3β-acetoxy-5α,16β,17β-pentaran-21-one) prepared during the course of this work is of especial interest because a compound having the same overall structure has been prepared by Engel and Lessard[18] by an entirely different route. The 16β-configuration was assigned to this compound on the basis

[18] Ch. R. Engel and J. Lessard, *J. Amer. Chem. Soc.* **85**, 638 (1963).

of (i) its marked laevorotation and (ii) the concept of preferred α-side attack; no configuration was proposed for the hydrogen atom at C-17. The physical constants quoted by the Canadian workers (m.p. 166–168°, $[\alpha]_D$ −102°) are in excellent agreement with those (m.p. 167°, $[\alpha]_D$ −109°) found by us for the 16β,17β-isomer, and differ markedly from those (m.p. 170·5°, $[\alpha]_D$ +113°) of the 16α,17α-isomer. Whilst we have not carried out a direct comparison of the two compounds, there seems little doubt that Engel and Lessards' product has the 16β,17β-configuration.

In Tables 2, 3 and 4 are presented data for many of the pentacyclic steroids and intermediates prepared in the course of this work.

EXPERIMENTAL

Optical rotations were determined on ca. 1% soln in chf at room temp. UV spectra were determined in EtOH soln on either a Beckmann DK2 or a Perkin–Elmer 350 spectrophotometer. IR spectra were measured on a Hilger H800 spectrophotometer fitted with either a NaCl or a CaF_2 prism. NMR spectra were measured in $CDCl_3$ soln, with TMS as internal standard, on a Perkin–Elmer 40 Mc/s spectrometer. ORD spectra were determined in MeOH or dioxan soln on a Bendix-Bellingham and Stanley Polarmatic 62 spectropolarimeter.

Preparation of 16-*hydroxymethylene*-17-*ketones* (Table 2)

MeONa was prepared from Na (10 parts) and dry MeOH (200 parts) and excess MeOH was removed under reduced press. A soln (or suspension) of the 17-ketone (10–15 parts) and ethyl orthoformate (10 parts) in dry benzene (200 parts) was added, the mixture was stirred under N for 1–2 hr at room temp followed by 1–2 hr under reflux. The mixture was poured into water, the benzene layer was separated and the aqueous layer was washed with several portions of ether. The aqueous layer was freed of ether by bubbling N throught it, and then acidified with dil H_2SO_4 or AcOH. The precipitated hydroxymethylene derivative was collected, washed with water and dried (yield ca. 80–95%). It could be used in this form for further transformations, a small portion only being crystallized from a suitable solvent for characterization.

Preparation of 16-3′-*oxobutyl*-17-*ketones* (Table 3).

To a soln of the 16-hydroxymethylene-17-ketone (5 parts) in pyridine (75–100 parts) was added, under N, freshly distilled methyl vinyl ketone (5 parts) and Et_3N (2·5 parts). The mixture was stirred at room temp overnight and the solvents were removed *in vacuo*. A solution of the residue in ether or dichloromethane was washed successively with dil HCl, dil KOHaq and water, dried (Na_2SO_4) and evaporated to dryness. A benzene soln of the residue was chromatographed on alumina (100 parts). Elution with benzene and benzene–ether (1:1) gave the 16-3′-oxobutyl-17-ketone which was crystallized in the usual way.

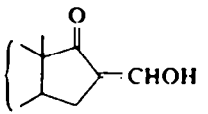
Cyclization of the 16-3′-*oxobutyl*-17-*ketones* (Table 4)

To a soln of the 16-3′-oxobutyl-17-ketone (5 parts) in EtOH (50–100 parts) was added, under N KOHaq (20%, 75 parts) and the mixture was refluxed for ca. 1 hr. The pentacyclic compound generally crystallized on cooling and/or dilution of the mixture with water and was collected and purified in the usual way. When no crystallization occurred, the reaction mixture was poured into water and the steroid was isolated with ether.

Isolation of 16-*formyl*-16-3′-*oxobutyl*-17-*ketones*

a. The condensation between 3,3-ethylenedioxy-11β-hydroxy-16-hydroxymethyleneandrost-5-en-17-one (26 g) and methyl vinyl ketone was carried out as described above. The residue obtained on evaporation of the liquids under reduced press was dissolved in benzene and the soln was kept overnight. A portion of the crystalline solid (24 g), m.p. 165–170°, which had separated was crystallized from acetone–hexane to give 3,3-ethylenedioxy-16β-formyl-11β-hydroxy-16α-3′-oxobutylandrost-5-en-17-one, m.p. 169·5–170°, $[\alpha]_D$ +82·9°, $\nu_{max}^{CHCl_3}$ 3615 (—OH), 1745 (C-17-ketone), 1714 cm^{-1} (formyl + oxobutyl ketones), NMR 0·5 (—CHO), 4·29 (C-6—H), 5·5 (11α-H), 6·05 (mult, ketal),

TABLE 2



Starting material		m.p.	$[\alpha]_D$	λ_{max} mμ(ε)	ν_{max} cm^{-1} (CH_2Cl_2)	Formula	Found C	Found H	Required C	Required H
3β-Hydroxy-6-methylandrost-5-en-17-one	[a]	178–179	−76·9	268 (15,050)	3611, 1710, 1635.	$C_{21}H_{30}O_2$	76·4	9·45	76·3	9·15
3β-Hydroxy-5α-androstan-17-one		229·5	+50·9	265 (11,438)	3250, 1704 1630.	$C_{20}H_{30}O_2$	74·8	9·5	75·4	9·5
3,3-Ethylenedioxy-11β-hydroxyandrost-5-en-17-one	[b]	224	−12·1	264 (16,480)	3430, 1702 1638, (1601)	$C_{23}H_{34}O_5$	69·7	8·25	69·55	8·05
3,3-Ethylenedioxy-11β-hydroxy-5α-androstan-17-one	[b]	218–220	+53	264 (11,300)	—	$C_{23}H_{36}O_5$	70·05	8·5	70·2	8·6
5α-Androstane-3β,11β-diol-17-one	[a]	dec above 250	−18·5	263 (12,500)	3550, 3275 1703, 1624.	$C_{19}H_{30}O_4$	71·9	9·0	71·8	9·05
6β-Hydroxy-3α,5-cyclo-5α-androstan-17-one		185–187	+64	265 (12,800)	3300, 1720 1650.	$C_{20}H_{28}O_3$	75·1	8·75	75·9	8·9

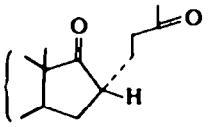
[a] Prepared by hydrolysis of the 3-acetate, cf. V. Grenville, D. K. Patel, V. Petrow, I. A. Stuart-Webb and D. M. Williamson, *J. Chem. Soc.* 4105 (1957).

[b] 17-Ketone not characterised.

[c] M. Harnik, *Israel. J. Chem.* **1**, 158 (1963).

[d] A. Butenandt and L. A. Suranyi, *Ber. Dtsch. Chem. Ges.* **75**, 591 (1942).

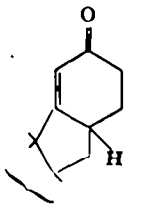
TABLE 3



Starting material		m.p.	$[\alpha]_D$	ν_{max} cm^{-1}	Formula	Found C	Found H	Required C	Required H
3β-Hydroxyandrost-5-en-17-one	[a]	156–157	+11·7	3606, 1730, 1708	$C_{22}H_{34}O_3$	76·65	9·25	77·05	9·55
corresponding acetate		127–128	+2·4	1734, 1720 (sh), 1240	$C_{24}H_{36}O_4$	75·45	9·35	74·95	9·05
3β-Acetoxy-6-methylandrost-5-en-17-one		156–157	−9·8	1736, 1724, 1240	$C_{24}H_{36}O_4$	75·3	9·25	75·15	9·15
3,3-Ethylenedioxy-11β-hydroxyandrost-5-en-17-one		173–174	+7·4	- -	$C_{23}H_{36}O_5$	72·4	8·55	72·1	8·7
3,3-Ethylenedioxyandrosta-5,9(11)-dien-17-one		129–130	+96·9	1730, 1715	$C_{23}H_{34}O_4$	75·1	8·5	75·3	8·6
3,3-Ethylenedioxy-11β-hydroxy-5α-androstan-17-one		182	+55	3660, 3475 1735, 1723	$C_{23}H_{38}O_5$	71·6	9·05	71·75	9·15
6β-Hydroxy-3α,5-cyclo-5α-androstan-17-one		142–144	+88	1735, 1720	$C_{22}H_{34}O_2$	76·6	9·3	77·05	9·55
3-Methoxyoestra-1,3,5(10)-trien-17-one	[b]	163–164	+137	1737, 1722 1612	$C_{23}H_{30}O_2$	78·25	8·65	77·95	8·55

[a] 16-Hydroxymethylene-17-ketone described by L. Ruzicka, V. Prelog and J. Battegay, *Helv. Chim. Acta* **31**, 1296 (1948).
[b] The corresponding 17-ketone is described in the experimental section; the 16-hydroxymethylene-17-ketone was not characterized.
[c] 16-Hydroxymethylene-17-ketone described by J. C. Bardham, *J. Chem. Soc.* 1848 (1936).

Table 4



Starting material	m.p. °C	$[\alpha]_D$ $CHCl_3$	λ_{max} mμ(ε)	ν_{max} cm^{-1}	Formula	Found C	Found H	Required C	Required H
3-β-Hydroxyandrost-5-en-17-one	191–192	−97·4	237 (16,260)	3623, 1678 1647.	$C_{19}H_{28}O_2$	80·75	9·1	81·15	9·45
corresponding acetate	206–207	−107·2	236 (16,980)	1735, 1675, 1643.	$C_{21}H_{30}O_3$	78·15	8·85	78·5	8·95
corresponding 4-en-3-one[a]	205–206	+70	236 (34,270)	1670, 1647 1622	$C_{19}H_{26}O_2$	81·55	8·7	81·6	8·9
3β-Hydroxy-6-methylandrost-5-en-17-one	196–197	−129·7	236 (15,400)	3620, 1675 1644	$C_{20}H_{30}O_2$	81·0	9·9	81·3	9·65
corresponding acetate	182–183	−111·5	236 (17,740)	1734, 1676, 1643.	$C_{22}H_{32}O_3$	79·0	9·0	78·75	9·15
corresponding 6α-methyl-4-en-3-one[a]	192–193	+41·2	238 (27,740)	1677, 1643 1620.	$C_{20}H_{28}O_2$	81·35	9·1	81·75	9·15
3β-Hydroxy-5α-androstan-17-one[b]	193	−32·8	236 (16,600)	3615, 1673 1643	$C_{19}H_{30}O_2$	80·3	10·15	80·65	10·0
3,3-Ethylenedioxy-11β-hydroxy-androst-5-en-17-one	241–242	−108·5	237 (11,500)	3380, 1677 1645	$C_{23}H_{34}O_4$	75·15	8·6	75·35	8·6
corresponding 4-en-3-one[c]	233–234	+57·5	239 (33,300)	3378, 1670 1650, 1612	$C_{21}H_{30}O_3$	77·95	8.45	77·95	8·5
corresponding 11-ketone[d]	244–245	+104	236 (31,900)	1708, 1666 1617	$C_{23}H_{32}O_5$	78·1	7·9	78·35	8·0

3,3-Ethylenedioxyandrosta-5,9-(11)-diene-17-one	189–190	−4·6	235 (15,800)	1674, 1643	$C_{20}H_{32}O_2$	78·9	8·5	78·9	8·5
corresponding 4-en-3-one[a]	263–264	+48·9	237·5 (32,800)	1664, 1607	$C_{20}H_{30}O_2$	82·25	8·2	82·1	8·4
3,3-Ethylenedioxy-11β-hydroxy-5α-androstan-17-one	225–226	−10·6	237 (17,569)	3660, 1681, 1648.	$C_{20}H_{34}O_4$	74·8	8·9	74·95	9·05
corresponding 3-ketone[a]	224–225	−12·7	237 (17,700)	3625, 3400 1715, 1677 1643.	$C_{19}H_{30}O_3$	77·2	8·9	77·5	9·05
5α-Androstane-3β,11β-diol-17-one[b]	230–232	−22·5	236·5 (16,880)	3400(broad) 1658, 1641	$C_{19}H_{34}O_3$	76·65	9·65	77·05	9·55
5β-Androstane-3α,11β-diol-17-one[c]	200	−10·4	237 (16,900)	3601, 1662, 1642.	$C_{19}H_{34}O_3 \cdot \frac{1}{2}H_2O$	75·15	9·3	75·15	9·6
6β-Hydroxy-3α,5-cyclo-5α-androstan-17-one	137–139	+5·65	235·5 (15,400)	3600, 1675 1645.	$C_{19}H_{30}O_3$	81·1	9·2	81·15	9·45
corresponding 6-ketone[d]	176–178	+23·7	235 (16,600)	1680, 1665 1640	$C_{19}H_{28}O_3$	81·3	8·9	81·6	8·95
3-Methoxyoestra-1,3,5(10)triene-17-one	241–242	−4·0	234 (24,390)	1665, 1610 1575, 1501.	$C_{19}H_{26}O_2$	81·6	8·65	82·1	8·4

[a] Prepared by Oppenauer oxidation of the foregoing 3β-hydoxy-5-ene.

[b] The intermediate 16-oxobutyl-17-ketone was not characterized.

[c] Prepared by mild acidic hydrolysis of the foregoing ketal.

[d] Preparared by oxidation of the foregoing 11β-hydroxy derivative with chromium trioxide in aqueous suplhuric acid and acetone.

[e] No intermediates were characterized: the unsubstituted 17-ketone has been described by H. L. Herzog, M. A. Jevnik, P. L. Perlman, A. Nobile and E. B. Hershberg, *J. Amer. Chem. Soc.* **75**, 266, (1953).

[f] Prepared by oxidation of the foregoing 6β-alcohol with chromium trioxide in pyridine.

7·88 (—CO—CH_3), 8·54 and 8·80 τ (C-19— and C-18—CH_3). (Found: C, 70·5; H, 8·0. $C_{26}H_{36}O_6$ requires: C, 70·25; H, 8·15%.)

A portion of this material was absorbed from benzene soln onto an alumina column and kept overnight. Elution with benzene gave, as the major product, 3,3-ethylenedioxy-11β-hydroxy-16α-3'-oxobutylandrost-5-en-17-one, needles from acetone–hexane, m.p. 168–170° (Table 2).

A further portion of the 16-formyl-3'-oxobutyl-17-ketone was treated with aq alc. KOH as described above for the cyclization of 16-3'-oxobutyl-17-ketones. The product was 3,3-ethylenedioxy-11β-hydroxy-16β-pentara-5,17(20)-diene-21-one, needles from methylene chloride–acetone (containing a trace of pyridine), m.p. 240° (Table 3).

b. 16-Hydroxymethyleneoestrone methyl ester (35 g) was condensed with methyl vinyl ketone in the usual way. Evaporation of the liquids under reduced press and crystallization of the residue from chf–hexane gave 16β-formyl-16α-3'-oxobutyl-3-methoxyoestra-1,3,5(10)-trien-17-one, m.p., 127·5°, $[\alpha]_D$ +217·4°, $\nu_{max}^{CHCl_3}$ 1745 (C-17-ketone), 1715 (formyl + oxobutyl ketones), 1610, 1575, 1500 cm^{-1} (3-methoxy-1,3,5-(10)-triene), NMR 0·5 (C-16—CHO), 3 (quartet, aromatic protons), 6·23 (C-3—OMe), 7·84 (—CO—CH_3) and 9·18 τ (C-18—CH_3). (Found: C, 75·65; H, 7·7. $C_{34}H_{46}O_4$ requires: C, 75·35; H, 7·9%.)

Isolation of the spirocyclic by-products

a. 3β-Hydroxyandrost-5-en-17-one-16-spiro-1'-cyclohexan-2'-ol-4'-one and 3β-hydroxyandrost-5-en-17-one-16-spiro-1'-cyclohex-2'-en-4'-one. The product obtained from 3β-hydroxy-16-hydroxymethyleneandrost-5-en-17-one (10 g) and methyl vinyl ketone was chromatographed in benzene solution on alumina (800 g). Elution with ether–benzene (1:1) and ether gave 3β-hydroxy-16α-3'-oxobutylandrost-5-en-17-one (6·5 g, see Table 2); elution with ether–MeOH (99:1) gave 3β-hydroxyandrost-5-en-17-one-16-spiro-1'-cyclohex-2'-en-4'-one (0·6 g) as needles from methylenechloride–hexane, m.p. 234°, $[\alpha]_D$ −237·5°, λ_{max} 218 (ε 7914), 250 (ε 5454) and 305 mμ (ε 809), $\nu_{max}^{CHCl_3}$ 3560 (—OH), 1740 (C-17-ketone), 1655, 1615 cm^{-1} (αβ-unsaturated ketone). (Found: C, 78·0; H, 8·55. $C_{24}H_{34}O_3$ requires: C, 78·22; H, 8·75%.) The acetate formed needles from acetone–hexane, m.p. 232-233°, $[\alpha]_D$ −222·8°, λ_{max} 218 (ε 7840), 250 (ε 5620) and 305 mμ (ε 796), ν_{max}^{Nujol} 1720–1735 (C-17-ketone + acetate), 1675, 1620 (αβ-unsaturated ketone) and 1250 cm^{-1} (acetate). (Found: C, 75·9; H, 8·55. $C_{26}H_{36}O_4$ requires: C, 76·05; H, 8·35%.) Further elution of the column with ether—MeOH (95:5) gave 3α-hydroxyandrost-5-en-17-one-16-spiro-1'-cyclohexan-2'-ol-4'-one (2·5 g) which crystallized from chf–acetone as rods, m.p. 239–240°. $[\alpha]_D$ +21·6°, $\nu_{max}^{CHCl_3}$ 3593, 3494 (OH) and 1720 cm^{-1} (1709 cm^{-1} in Nujol). (Found: C, 74·25; H, 8·7. $C_{24}H_{34}O_4$ requires: C, 74·55; H, 8·85%.) On acetylation (Ac_2O–pyridine, 100°, ½hr), the acetate, m.p. 230°, of the αβ-unsaturated ketone described above was obtained.

b. 3,3-*Ethylenedioxy*-11β-*hydroxyandrost*-5-*en*-17-*one*-*one*-16-*spiro*-1'-*cyclohex*-2'-*en*-4'-*one*. The condensation between 3,3-ethylenedioxy-11β-hydroxy-16-hydroxymethyleneandrost-5-en-17-one (60 g) and methyl vinyl ketone was carried out as described above and a portion (50 g) of the crude 16β-formyl-16α-3'-oxobutyl-17-ketone was chromatographed in benzene soln on alumina (1 kg). Elution with benzene and benzene–ether (1:1) gave 3,3-ethylenedioxy-11β-hydroxy-16α-3'-oxobutylandrost-5-en-17-one (26 g, m.p. 170°, see Table 2). Elution with ether and ether–MeOH (99:1) gave the spirocyclic unsaturated ketone (3 g) which was crystallized from chf–acetone, m.p. 280°, $[\alpha]_D$ −210·1°, λ_{max} 252 (ε 6100) and 307 mμ (ε 772), ν_{max} 1738 (C-17-ketone), 1678 and 1612 cm^{-1} (αβ-unsaturated ketone). (Found: C, 73·0; H, 7·85. $C_{26}H_{34}O_6$ requires: C, 73·2; H, 8·05%.)

c. 3-*Methoxyoestra*-1,3,5(10)-*trien*-17-*one*-16-*spiro*-1'-*cyclohex*-2'-*en*-4'-*one*. The condensation between 16-hydroxymethyleneoestrone methyl ether (5 g) and methyl vinyl ketone was carried out as described above and the crude product was chromatographed in benzene soln on alumina (150 g). Elution with benzene gave 3-methoxy-16α-3'-oxobutyloestra-1,3,5(10)-trien-17-one (3·6 g, see Table 2). Elution with benzene–ether (1:1) gave the spirocyclic unsaturated ketone (0·15 g) which was crystallized from acetone–hexane, m.p. 198–199°, $[\alpha]_D$ −92·9°, λ_{max} 250 (ε 6063), 278 (ε 2591), 287 (ε 2496) and 307 mμ (ε 846), $\nu_{max}^{CHCl_3}$ 1740 (C-17-ketone) and 1680, 1610 cm^{-1} (αβ-unsaturated ketone). (Found: C, 78·85; H, 7·54. $C_{24}H_{32}O_3$ requires: C, 79·1; H, 7·75%.)

d. 3α,5-*Cyclo*-5α-*androstan*-6β-*ol*-17-*one*-16-*spiro*-1'-*cyclohexan*-2'-ol-4-*one* and 3α,5-*cyclo*-5α-*androstan*-6β-ol-17-*one*-16-*spiro*-1'-*cyclohex*-2'-en-4'-*one*. The condensation between 16-hydroxymethylene-3α,5-cyclo-5α-androstan-6β-ol-17-one (8·5 g) and methyl vinyl ketone was carried out as described above and the product was chromatographed in benzene soln on alumina (250 g). Elution

with benzene gave 16α-3'-oxobutyl-3α,5-cyclo-5α-androstan-6β-ol-17-one (3 g, see Table 2). Elution with benzene and benzene–ether (1:1) gave the spirocyclic unsaturated ketone (1 g) m.p. 190–192° (from acetone–hexane), $[\alpha]_D$ −132·8°, λ_{max} 219 (ε, 7739), 251 (ε, 5196) and 305 mμ (ε, 752), $\nu_{max}^{CHCl_3}$ 3620 (C-6-hydroxyl), 1735 (C-17-ketone) and 1676, 1615 cm⁻¹ (αβ-unsaturated ketone). (Found: C, 77·4; H, 8·75. $C_{34}H_{52}O_3 \cdot \frac{1}{2}H_2O$ requires: C, 77·3; H, 8·8%.)

Further elution of the column with ether and ether–MeOH (95:5) gave the spirocyclic β-ketol (0·3 g) which crystallized from acetone–hexane, m.p. 235–240° dec, $[\alpha]_D$ +87·2°, no UV absorption, $\nu_{max}^{CHCl_3}$ 3615 and 1719 cm⁻¹ (1725 and 1711 cm⁻¹ in Nujol). (Found: C, 74·8; H, 9·05. $C_{34}H_{54}O_4$ requires: C, 74·55; H, 8·85%.)

11β-Hydroxy-16α-3'-oxobutylandrost-4-ene-3,17-dione

A soln of 3,3-ethylenedioxy-11β-hydroxy-16α-3'-oxobutylandrost-5-en-17-one (1 g) in AcOH (15 ml) and water (5 ml) was warmed on the steam bath for 20 min. Dilution with water and crystallization of the ppt from acetone–hexane gave 11β-hydroxy-16α-3'-oxobutylandrost-4-ene-3,17-dione (0·7 g) as prisms, m.p. 174°, $[\alpha]_D$ +160·4°, λ_{max} 241 mμ (ε, 16,020), ν_{max}^{Nujol} 3376 (OH), 1736 (C-17-ketone), 1708 (side-chain ketone), 1646 and 1608 cm⁻¹ (4-en-3-one). (Found: C, 74·4; H, 8·7. $C_{23}H_{32}O_4$ requires: C, 74·15; H, 8·65%.)

16α-3'-Oxobutyl-5β-androstan-11β-ol-3,17-dione

To a soln of the foregoing 4-en-3-one (5·8 g) in dioxan (200 ml) was added a soln of KOH (1·5 g) in dry MeOH (20 ml) and the mixture was hydrogenated at NTP over pre-reduced 5% Pd–charcoal (3 g); H uptake (ca. 1 eq) was complete in 1 hr. The catalyst was removed and the soln was evaporated to dryness under reduced press. A soln of the residue in ether (containing some methylene chloride) was washed with water, dried (Na_2SO_4), and evaporated. Crystallization of the residue from acetone gave the saturated trione as needles, m.p. 212–213°, $[\alpha]_D$ +86·9°, no UV absorption, ν_{max} 3437 (OH), 1735 (17-ketone), 1712 (3-ketone) and 1690 cm⁻¹ (H-bonded side-chain ketone), NMR 7·87 (side-chain $CO{\cdot}CH_3$), 8·65 (OH), 8·74 (C-19—Me) and 8·91 τ (C-18—Me). (Found: C, 73·35; H, 9·05. $C_{23}H_{34}O_4$ requires: C, 73·75; H, 9·15%.)

11β-Hydroxy-5β, 16β-pentar-17(20)-ene-3,21-dione

The foregoing 16-oxobutyl compound was cyclized in the usual way. The product crystallized from acetone–hexane to give the pentarane as laths, m.p. 216–217°, $[\alpha]_D$ −3·5°, λ_{max} 236·5 mμ (ε, 16,900). ν_{max} 3605 (OH), 1711 (3-ketone), 1665 and 1633 cm⁻¹ (αβ-unsaturated ketone), NMR 4·38 (doublet, C-20—H), 8·37 (OH), 8·70 (C-19—Me) and 8·78 τ (C-18—Me). (Found: C, 77·1; H, 8·8. $C_{23}H_{32}O_3$ requires: C, 77·5; H, 9·05%.)

3β-Acetoxypentara-5,17(20),21,23-tetraen-21-ol

a. A soln of 3β-acetoxy-16β-pentara-5,17(20)-dien-21-one (2 g) and DDQ (1·4 g, 1·2 eq) in dry dioxan (50 ml) was refluxed for 5½ hr. The soln was cooled and the precipitated hydroquinone was filtered off. The filtrate was diluted with ether, washed with Na_2CO_3aq and water, dried (Na_2SO_4) and evaporated under reduced press. Crystallization of the residue from chf–MeOH gave the phenol (0·8 g) as needles, m.p. 280°, $[\alpha]_D$ −68°, λ_{max} 281 mμ (ε, 3500), $\nu_{max}^{CHCl_3}$ 3560 (C-21—OH), 1731 (C-3—OAc) and 1615, 1593 cm⁻¹ (aromatic ring). (Found: C, 78·9; H, 8·75. $C_{28}H_{32}O_3$ requires: C, 78·9; H, 8·5%.)

The 3,21-diacetate (Ac_2O–pyridine, 100°, ½ hr) formed needles from MeOH m.p. 159°, $[\alpha]_D$ −54·8°, λ_{max} 266·5 (ε, 1470) and 273 mμ (δ, 1430), $\nu_{max}^{CCl_4 \cdot CS_2}$ 1768, 1208 (phenolic OAc) and 1739, 1240 cm⁻¹ (aliphatic OAc), NMR: ca. 3·0 (aromatic protons), 7·72 (phenolic OAc), 7·96 (C-3 β-OAc), 8·90 (C-18—Me) and 9·03 τ (C-19—Me). (Found: C, 76·25; H, 8·1. $C_{27}H_{34}O_4$ requires: C, 76·75; H, 8·1%.)

The methyl ether (3βOH) (Me_2SO_4–methanolic KOHaq) formed plates from MeOH, m.p. 163–164°, $[\alpha]_D$ −69°, λ_{max} 226 (ε, 6870), 279 (ε, 3170) and 286 mμ (ε, 2720), $\nu_{max}^{CHCl_3}$ 3610, 1676 and 1610 cm⁻¹, NMR: 2·9–3·5 (aromatic ABX system), 4·55 (C-6—H), 6·21 (C-21—OMe), 8·92 (C-19—Me) and 9·06 τ (C-18—Me). (Found: C, 82·1; H, 8·95. $C_{24}H_{32}O_3$ requires: C, 81·75; H, 9·15%.)

b. A soln of 3β-acetoxy-16β-pentara-5,17(20)-dien-21-one (2 g) and chloranil (5 g) in dry t-butanol (50 ml) was refluxed for 3½ hr. After keeping overnight at room temp, the excess quinone

was filtered off and the filtrate was concentrated under reduced press. The residue was diluted with ether, washed with 5% KOHaq and water, dried (Na_2SO_4) and evaporated to dryness. Crystallization of the residue from chf–MeOH gave the phenol as needles, m.p. 275–277°, identical with the product obtained using DDQ.

11β-Hydroxy-16α-3′-oxobutylandrosta-1,4-diene-3,17-dione

A soln of 11β-hydroxy-16α-3′-oxobutylandrost-4-ene-3,17-dione (1·3 g) and DDQ (1·3 g, 1·3 eq) in dry dioxan (50 ml) was refluxed for 6 hr. After cooling, the precipitated hydroquinone was filtered off, the filtrate was diluted with ether and washed with 5% KOHaq and water. Evaporation of the dried (Na_2SO_4) extract and crystallization of the residue from acetone–hexane gave the dienedione (0·6 g) as needles, m.p. 226·5°, $[\alpha]_D$ +85·2°, λ_{max} 242 mμ (ε, 14,264), ν_{max}^{Nujol} 3375 (OH), 1739 (C-17-ketone), 1715 (side-chain ketone), 1657, 1613 and 1603 cm^{-1} (1,4-dien-3-one). (Found: C, 74·65; H, 8·3. $C_{23}H_{30}O_4$ requires: C, 74·55; H, 8·15%.)

11β-Hydroxy-16β-pentara-1,4,17(20)-triene-3,21-dione

The foregoing 1,4-dien-3-one (1 g) was cyclized as described earlier. Crystallization of the product from acetone–hexane gave the pentarane (0·55 g) as laths, m.p. 208–209°, $[\alpha]_D$ +15·8°, λ_{max} 238 mμ (ε, 28,700), ν_{max}^{Nujol} 3330 (OH), 1662, 1643, 1612 and 1597 cm^{-1} (unsaturated ketones). (Found: C, 78·05; H, 7·6. $C_{23}H_{28}O_3$ requires: C, 78·35; H, 8·0%.)

11β-Hydroxy-16α-3′-oxobutylandrosta-4,6-diene-3,17-dione

A soln of 11β-hydroxy-16α-3′-oxobutylandrost-4-ene-3,17-dione (2 g) and chloranil (5 g) in dry t-butanol (50 ml) was refluxed for 3 hr. After cooling, excess quinone was filtered off, the filtrate was diluted with ether and washed with 5% KOHaq and water. Evaporation of the dried (Na_2SO_4) extract and crystallization of the residue from acetone–hexane gave the dienedione (1·1 g) as needles, m.p. 221–222°, $[\alpha]_D$ +133·6°, λ_{max} 282 mμ (ε, 24,400), ν_{max}^{Nujol} 3520 (OH), 1741 (C-17-ketone), 1721 (side-chain ketone), 1640, 1616 and 1577 cm^{-1} (4,6-dien-3-one). (Found: C, 74·3; H, 8·25. $C_{23}H_{30}O_4$ requires: C, 74·55; H, 8·15%.)

11β-Hydroxy-16β-pentara-4,6,17(20)-triene-3,21-dione

The foregoing 4,6-dien-3-one (1 g) was cyclized as described earlier. The product crystallized from acetone to give the pentarane (0·65 g) as needles, m.p. 263–264°, $[\alpha]$ −44·4°, λ_{max} 237 (ε, 16,200) and 280 mμ (ε, 22,700). (Found: C, 78·15; H, 8·0. $C_{23}H_{28}O_3$ requires: C, 78·35; H, 8·0%.)

*3,3-Ethylenedioxyandrosta-5,9(11)-dien-17-one**

A soln of 3,3-ethylenedioxy-11β-hydroxyandrost-5-en-17-one (29 g) in pyridine (250 ml) was added, dropwise at 0°, to a stirred soln of $POCl_3$ (60 ml) and H_3PO_4 (5 ml) in pyridine (250 ml). After stirring for a further 2 hr at 0°, the soln was kept overnight at room temp and poured into water. Crystallization of the ppt (24 g) from acetone–hexane gave 3,3-ethylenedioxyandrosta-5,9(11)-dien-17-one as needles, m.p. 194–195°, $[\alpha]_D$ +101·3° (dioxan), no UV absorption. (Found: C, 76·3; H, 8·5. $C_{21}H_{30}O_3$ requires: C, 76·8; H, 8·6%.)

*9α-Bromo-11β-hydroxy-16β-pentara-4,17(20)-diene-3,21-dione**

A soln of 16β-pentara-4,9(11),17(20)-triene-3,21-dione (1·5 g, see Table 4) in dioxan (75 ml), water (15 ml) and 70% perchloric acid (0·75 ml) was stirred with N-bromacetamide (1·6 g) for 1 hr at room temp. Na_2SO_3aq was added to discharge the colour and the ppt was collected. The bromhydrin formed needles (1·5 g) from CH_2Cl_2–MeOH, m.p.—indefinite decomposition, $[\alpha]_D$ +58·9°, λ_{max} 239 mμ (ε, 32,600), $\nu_{max}^{CH_2Cl_2}$ 3615 (C-11—OH). 1662 and 1612 cm^{-1} (αβ-unsaturated ketones). (Found: C, 64·1; H, 7·1; Br, 19·1. $C_{23}H_{31}BrO_5$ requires: C, 63·7; H, 6·7; Br, 18·4%.)

*9β,11β-Epoxy-16β-pentara-4,17(20)-diene-3,21-dione**

A soln of the foregoing bromhydrin (2·4 g) and anhyd AcOK (2·5 g) in EtOH (200 ml) was refluxed for 1 hr. The soln was concentrated under reduced press and diluted with water. The ppt was

* Experiment carried out by M. Howarth.

collected and chromatographed in benzene soln on silica (200 g). Elution with benzene–ether mixtures gave the 9β,11β-oxide, (0·8 g), m.p. 221–222° (from acetone–hexane), $[\alpha]_D$ −64·8°, λ_{max} 238 mμ (ε, 31,130), $\nu_{max}^{CCl_4}$ 1675, 1642 and 1622 cm^{-1}. (Found: C, 78·15; H, 8·1. $C_{23}H_{30}O_3$ requires: C, 78·4; H, 8·0%.)

*9α-Fluoro-11β-hydroxy-16β-pentara-4,17(20)-diene-3,21-dione**

To a cooled (0°) soln of the foregoing epoxide (1·25 g) in dimethylformamide (7·5 ml) was added anhydrous HF (7·5 ml). The mixture was kept at 0° for 6 hr and overnight at room temp. The oil obtained on pouring the mixture into K_2CO_3aq was extracted into CH_2Cl_2, the extract was washed (H_2O), dried (Na_2SO_4) and evaporated. Crystallization of the residue from benzene gave the fluorhydrin (0·7 g) as needles, m.p. 243–244°. $[\alpha]_D$ +27·8°, λ_{max} 237 mμ (ε, 31,630), $\nu_{max}^{CH_2Cl_2}$ 3614, 1667, 1624 cm^{-1}. (Found: C, 73·85; H, 7·9. $C_{23}H_{29}FO_3$ requires: C, 74·15; H, 7·85%.)

11β-Hydroxy-3-methoxy-16β-pentara-3,5,17(20)-trien-21-one

A suspension of 11β-hydroxy-16β-pentara-4,17(20)-diene-3,21-dione (1·4 g) in dry THF (15 ml), trimethyl orthoformate (1·2 ml) and MeOH (1 ml) containing toluene-*p*-sulphonic acid (0·04 g) was stirred at room temp for 25 min, during which time the steroid dissolved. Pyridine (1 ml) and water (ca. 50 ml) were added and the ppt was collected. Crystallization from CH_2Cl_2–MeOH (containing a trace of pyridine) gave the enol ether (0·7 g) as needles, m.p. 216–219°, $[\alpha]_D$ −247·7°, λ_{max} 238·5 mμ (ε, 32,500), NMR 4·3 (d, J ca. 2 c/s, C-20—H), 4·87 (m, C-4 + C-6—H), 6·42 (C-3—OMe), 8·76 τ (C-18 + C-19—Me). (Found: C, 77·65; H, 8·35. $C_{24}H_{32}O_3$ requires: C, 78·2; H, 8·75%.)

6-Formyl-11β-hydroxy-3-methoxy-16β-pentara-3,5,17(20)-trien-21-one

To a soln of the Vilsmeier reagent prepared from $POCl_3$ (1·3 ml) and dimethylformamide (3 ml) in CH_2Cl_2 (20 ml) was added, at 0°, a soln of the foregoing enol ether (1·8 g) in CH_2Cl_2 (20 ml, containing a few drops of pyridine) and the mixture was stirred at 0° for 15 min. NaOAcaq (10%, 100 ml) and ether were added, the aqueous phase was separated, the ether was washed with $NaHCO_3$aq and water, dried (Na_2SO_4) and evaporated. Crystallization of the residue from MeOH gave the 6-formyl enol ether (0·65 g) as needles, m.p. 267–268°, $[\alpha]_D$ −184·5°, λ_{max} 238 (ε, 23,400) and 322 mμ (ε, 16,800), ν_{max} 3530 (OH), 1656 (C-21-ketone), 1619 and 1600 cm^{-1} (C-6-formyl enol ether). (Found: C, 75·3; H, 8·1. $C_{25}H_{32}O_4$ requires: C, 75·7; H, 8·15%.)

11β-Hydroxy-6-methylene-16β-pentara-4,17(20)-diene-3,21-dione

To a soln of the foregoing 6-formyl enol ether (0·3 g) in THF (6 ml) was added lithium borohydride (0·015 g) and the mixture was kept at room temp for 5 min. The product was precipitated with water and extracted into ether. Evaporation of the washed (H_2O) and dried (Na_2SO_4) extract left a residue which was dissolved in 90% AcOH (5 ml) and kept at 50° for 10 min. Dilution with water and crystallization of the ppt from MeOH gave the 6-methylene derivative (0·1 g) as needles, m.p. decomposes above 245°, $[\alpha]_D$ +251·8°, λ_{max} 240 (ε, 24,400) and λ_{inflex} 265 mμ (ε, 11,800), NMR 4·14 (C-4—H), 4·37 (C-20—H), ca. 4·97 (AB quartet, >=CH_2), 8·18 (C-11 β-OH), 8·61 (C-19—Me), and 8·75 τ (C-18—Me). (Found: C, 78·25; H, 7·9. $C_{24}H_{30}O_3$ requires: C, 78·65; H, 8·25%.)

21,21-Ethylenedioxy-3-methoxy-19-norpentara-1,3,5(10),16-tetraene

A soln of 3-methoxy-19-nor-16β-pentara-1,3,5(10),17(20)-tetraen-21-one (6·2 g) in ethyl methyl dioxolan (120 ml) containing toluene-*p*-sulphonic acid (0·1 g) was slowly distilled over 3 hr. Pyridine (1 ml) and benzene were added, the mixture was washed with water, dried (Na_2SO_4) and evaporated under reduced press. Crystallization of the residue from MeOH (containing a trace of pyridine) gave the ketal (5 g) as prisms, m.p. 110–111°, $[\alpha]_D$ +7·3°, NMR ca. 3 (m, aromatic protons), 6·0 (ketal), 6·23 (C-3—OMe) and 9·22 τ (C-18—Me). (Found: C, 78·5; H, 8·4. $C_{24}H_{30}O_3$ requires: C, 78·9; H, 8·5%.)

19-Nor-16α-pentara-4,17(20)-diene-3,21-dione

A soln of the above ketal (4 g) in THF (250 ml) was added to a soln of Li (1 g) in liquid ammonia (200 ml) and the mixture was stirred under reflux for 4 hr. Ammonium chloride (10 g) was added

and the ammonia was allowed to evaporate overnight. Ether and water were added to the residue, the ether layer was separated, washed with water, dried (Na_2SO_4) and evaporated. A soln of the residue (ca. 3 g) in acetone (50 ml) was refluxed with toluene-*p*-sulphonic acid (0·25 g) for 3 hr, and then poured into dil Na_2CO_3aq. The product was isolated with ether and chromatographed onto alumina (150 g) in benzene sol. Elution with benzene–ether (4:1) gave small quantities of products retaining an aromatic ring A; elution with benzene–ether (2:3) gave crystalline materials which were combined and crystallized from MeOH aq to give 19-nor-16α-pentara-4,17(20)-diene-3,21-dione (0·35 g) as laths, m.p. 173·5°, $[\alpha]_D$ +123·9°, λ_{max} 241 mμ (ε, 33,100), NMR 4·13 (m, C-4 and C-20 protons) and 9·02 τ (C-18—Me). (Found: C, 81·1; H, 8·55. $C_{21}H_{28}O_2$ requires: C, 81·45; H, 8·7%.)

3-*Methoxy*-19-*nor*-16β-*pentara*-2,5(10),17(20)-*trien*-21-*one*

A suspension of 3-methoxyoestra-2,5(10)-dien-17-one (19·5 g) in dry benzene (500 ml) was added to MeONa (prepared from 5g Na) and ethyl formate (30 ml) and the mixture was stirred at room temp for 1 hr. More formate (10 ml) was added, the mixture was refluxed for 1½ hr, cooled, and the product was isolated as described earlier. The crude product (14·5 g) was dissolved in dry pyridine (150 ml), methyl vinyl ketone (10 ml) and Et_3N (5 ml) were added and the mixture was kept under N at room temp for 16 hr. The solvents were removed *in vacuo*, the residue was dissolved in EtOH (200 ml), a soln of KOH (30 g) in water (100 ml) was added and the soln was refluxed for 30 min. After cooling, the ppt was collected and crystallized from CH_2Cl_2—MeOH (containing a few drops of pyridine) to give 3-methoxy-19-nor-16β-pentara-2,5(10),17(20)-trien-21-one (10·5 g) as plates, m.p. 198°, $[\alpha]_D$ +79·3°, λ_{max} 234·5 mμ (ε, 18,400), $\nu_{max}^{CCl_4}$ 1695 (one band of 3-OMe-2,5(10)-diene d), 1674 and 1642 cm^{-1} (17(20)-en-21-one), NMR 4·31 (d, J 2 c/s, C-20—H), 5·32 (C-2—H), 6·44 (C-3—OMe) and 9·04 τ (C-18—Me). (Found: C, 81·6; H, 9·1. $C_{23}H_{30}O_2$ requires: C, 81·6; H, 8·95%.)

19-*Nor*-16β-*pentara*-4,17(20)-*diene*-3,21-*dione*

A soln of the foregoing enol ether (5 g) in MeOH (250 ml) was refluxed with a soln of conc HCl (30 ml) and water (30 ml) for 30 min. Dilution of the mixture with water, and crystallization of the ppt from CH_2Cl_2–MeOH gave 19-nor-16β-pentara-4,17(20)-diene-3,21-dione, m.p. 179°, $[\alpha]_D$ −22·7°, λ_{max} 238 mμ (ε, 33,600), NMR 4·11 (C-4—H), 4·29 (d, J 2·3 c/s, C-20—H) and 8·98 τ (C-18—Me). (Found: C, 81·0; H, 8·85. $C_{21}H_{28}O_2$ requires: C, 81·45; H, 8·7%.)

21,21-*Ethylenedioxypentara*-5,16-*dien*-3β-*ol*

A suspension of 3β-hydroxy-16β-pentara-5,17(20)-dien-21-one (2 g) in ethylene glycol (100 ml) containing toluene-*p*-sulphonic acid (0·05 g) was slowly distilled under reduced press (ca. 2 mm) for 1 hr (ca. 25 ml distillate); the steroid dissolved within 10 min and the product separated shortly afterwards. The suspension was cooled, neutralized with pyridine (ca. 5 ml) and the ppt collected. Crystallization from MeOH gave the ketal (1·3 g) as needles, m.p. 190°, $[\alpha]_D$ −67°, no UV absorption, NMR spectrum 4·6 (C-6—H, 1 only), 6·05 (—CH_2— of ketal), 8·05 (OH), 8·97 (C-19—Me) and 9·23 τ (C-18—Me). (Found: C, 78·15; H, 9·4. $C_{23}H_{36}O_3$ requires: C, 78·1; H, 9·45%.)

3β-*Hydroxy*-16α-*pentara*-5,17(20)-*diene*-21-*one*

A soln of the foregoing ketal (2 g) in acetone (60 ml) and water (5 ml) containing toluene-*p*-sulphonic acid (0·25 g) was refluxed for 8 hr. Ether (500 ml) was added, the soln was washed with Na_2CO_3aq and water, dried (Na_2SO_4) and evaporated to dryness. Crystallization of the residue from acetone gave 3β-hydroxy-16α-pentara-5,17(20)-dien-21-one (1·2 g) as laths, m.p. 212°, $[\alpha]_D$ +3°, λ_{max} 242 mμ (ε, 15,200), $\nu_{max}^{CH_2Cl_2}$ 3674, 3594 (OH), 1659 and 1606 cm^{-1} (αβ-unsaturated ketone) NMR 4·17 (C-20—H), 4·56 (C-6—H), 8·08 (OH), 8·96 (C-19—Me) and 9·08 τ (C-18—Me), ORD $[\phi]_{379}$ −1710°; $[\phi]_{361\cdot5}$ −1280°; $[\phi]_{344}$ −1550°; $[\phi]_{343}$ +450° (infl.); $[\phi]_{338}$ +2610° (infl.); $[\phi]_{316}$ +3690° (infl.) and $[\phi]_{301}$ +3950° (infl.) (*c*, 0·099 in dioxan). (Found: C, 79·4; H, 9·55. $C_{23}H_{32}O_3 \cdot \frac{1}{2}H_2O$ requires: C, 79·05; H, 9·5%.)

By comparison, 3β-hydroxy-16β-pentara-5,17(20)-dien-21-one (see Table 4) had the following ORD spectrum: $[\phi]_{344}$ +1400°; $[\phi]_{338}$ +100°; $[\phi]_{320}$ +1020°; $[\phi]_{306}$ −2550°; $[\phi]_{298}$ −2280°; $[\phi]_{295}$ −5750° (infl.); (*c*, 0·066 in dioxan).

21,21-*Ethylenedioxy*-5α-*pentar*-16-*en*-3β-*ol*

A suspension of 3β-hydroxy-5α,16β-pentar-17(20)-en-21-one (6 g) in ethylene glycol (200 ml) containing toluene-*p*-sulphonic acid (0·15 g) was slowly distilled under reduced press (ca. 2 mm) for 2 hr; after ca. 45 min the steroid had dissolved and the product precipitated soon afterwards. The solution was cooled, neutralized with pyridine (ca. 5 ml) and diluted with water. The ppt was collected and crystallized from CH_2Cl_2–MeOH to give the ketal (5·7 g) as plates, m.p. 194°, $[\alpha]_D$ +0·9°, no UV absorption, NMR 6·01 (—CH_2— of ketal), 7·68 (OH), 9·16 (C-19—Me) and 9·27 τ (C-18—Me). (Found: C, 77·2; H, 10·15; $C_{23}H_{36}O_3$ requires: C, 77·65; H, 9·9%.)

3β-*Hydroxy*-5α,16α-*pentar*-17(20)-*en*-21-*one*

A soln of the foregoing ketal (4 g) in acetone (90 ml) and water (10 ml) was refluxed with toluene-*p*-sulphonic acid (2 g) for 3 hr. Pyridine (3 ml) and water (10 ml) were added and some of the acetone was boiled off. The mixture was cooled, the ppt was collected and crystallized from CH_2Cl_2–acetone to give 3β-hydroxy-5α,16α-pentar-17(20)-en-21-one (3·1 g), m.p. 180–181°, $[\alpha]_D$ +71·3°, λ_{max} 242 mμ (ε, 16,000), ν_{max}^{Nujol} 3499, 3268 (OH), 1666 and 1644 cm^{-1} (αβ-unsaturated ketone), NMR 4·18 (d, J 2 c/s, C-20—H), 9·11 (C-18—Me) and 9·16 τ (C-19—Me), ORD $[\phi]_{371\cdot5}$ −4990°, $[\phi]_{343}$ −3420°; $[\phi]_{314}$ −4290°; $[\phi]_{343}$ +2660° (infl.); $[\phi]_{299}$ +10,080° (infl.); $[\phi]_{300}$ +15,200° (infl.); (*c*, 0·038 in dioxan). (Found: C, 78·4; H, 9·85. $C_{23}H_{34}O_3.\frac{1}{2}H_2O$ requires: C, 78·6; H, 10·05%.)

By comparison, 3β-hydroxy-5α,16β-pentar-17(20)-en-21-one (see Table 4) had the following ORD spectrum: $[\phi]_{344}$ +2780; $[\phi]_{314}$ +1660°; $[\phi]_{311}$ +2250°; $[\phi]_{328}$ −1490° (infl.); $[\phi]_{288}$ −4960° (infl.); $[\phi]_{313}$ −6660° (infl.); (*c*, 0·034 in dioxan).

3β-*Acetoxy*-16β,17β-*pentar*-5-*en*-21-*one*

A soln of 3β-hydroxy-16β-pentara-5,17(20)-dien-21-one (2·3 g) in EtOH (100 ml) was hydrogenated at NTP over pre-reduced 5% Pd–charcoal (0·2 g); H uptake virtually ceased after 40 min (190 ml, 1·3 eq). After removal of the catalyst, the soln was evaporated to dryness and the residue was acetylated (Ac_2O-pyridine, 100°, 2 hr). Crystallization of the product from acetone and CH_2Cl_2—MeOH gave 3β-acetoxy-16β,17β-pentar-5-en-21-one (1·7 g) as plates, m.p. 218°, $[\alpha]_D$ −179·2°, no UV absorption, $\nu_{max}^{CCl_4,CS_2}$ 1733, 1245 (acetate) and 1715 cm^{-1} (C-21 ketone), NMR 4·6 (d, C-6—H), 7·96 (acetate), 8·97 (C-19—Me) and 9·13 τ (C-18—Me). (Found: C, 78·2; H, 9·55. $C_{26}H_{36}O_3$ requires: C, 78·1; H, 9·45%.) Hydrolysis of the foregoing acetate with alcoholic KOHaq (room temp, 3 hr) gave the 3β-alcohol, plates from MeOH, m.p. 186°, $[\alpha]_D$ −200·1°, NMR 4·6 (d, C-6—H), 7·85 (OH + H_2O), 8·99 (C-19—Me) and 9·14 τ (C-18—Me), ORD $[\phi]_{300}$ −9530°; $[\phi]_{268}$ +7800°; a, −173° (*c*, 0·087 in MeOH). (Found: C, 77·15; H, 10·05. $C_{24}H_{34}O_3$. H_2O requires: C, 77·6; H, 10·05%.)

3β-*Hydroxy*-16α,17α-*pentar*-5-*en*-21-*one*

A soln of 3β-hydroxy-16α-pentara-5,17(20)-dien-21-one (1·5 g) in EtOH (100 ml) was hydrogenated at NTP over pre-reduced Pd–charcoal (5%, 0·2 g); H uptake was essentially complete within 15 min (110 ml, 1·1 eq). After removal of the catalyst, the solvent was evaporated *in vacuo* and the residue was crystallized from CH_2Cl_2–MeOH to give 3β-hydroxy-16α,17α-pentar-5-en-21-one (1·2 g) as needles, m.p. 223°, $[\alpha]_D$ +73°, no UV absorption, NMR 4·55 (m, C-6—H), 8·47 (OH), 8·97 (C-19—Me) and 9·22 τ (C-18—Me), ORD $[\phi]_{300}$ +9970°; $[\phi]_{267}$ −11,760°; a, 217·3° (*c*, 0·077 in MeOH). (Found: C, 80·55; H, 10·1. $C_{24}H_{34}O_3$ requires: C, 80·65; H, 10·0%.)

The 3β-acetate (Ac_2O–pyridine, room temp, overnight) formed needles from aqueous MeOH, m.p. 188°, $[\alpha]_D$ +55°, $\nu_{max}^{CCl_4,CS_2}$ 1733, 1238 (acetate) and 1716 cm^{-1} (C-21 ketone), NMR 4·57 (m C-6—H), 7·8 (acetate), 8·97 (C-19—Me) and 9·22 τ (C-18—Me). (Found: C, 78·55; H, 9·5. $C_{26}H_{36}O_3$ requires: C, 78·1; H, 9·45%.)

3β-*Hydroxy*-5α,16β,17β-*pentaran*-21-*one*

A soln of 3β-hydroxy-5α,16β-pentar-17(20)-en-21-one (1·8 g) in EtOH (100 ml) was hydrogenated at NTP over pre-reduced Pd–charcoal (5%, 0·16 g); H uptake was complete in 20 min (145 ml, 1·1 eq). After removal of the catalyst, the soln was evaporated to dryness and the residue was crystallized from CH_2Cl_2–acetone to give 3β-hydroxy-5α,16β,17β-pentaran-21-one (1·35 g) as needles, m.p. 190°, $[\alpha]_D$ −95·1°, no UV absorption below 260 mμ, NMR 8·35 (OH) and 9·18 τ (C-18 + C-19—Me), ORD $[\phi]_{310}$ −8280°; $[\phi]_{266}$ +8510°; a, 168° (*c*, 0·096 in MeOH). (Found: C, 80·45; H, 10·65. $C_{24}H_{36}O_3$ requires: C, 80·2; H, 10·55%.)

The 3β-acetate (Ac_2O–pyridine, room temp, overnight) formed laths from aqueous MeOH, m.p. 167°, $[\alpha]_D$ −109·1°; $\nu_{max}^{CCl_4:CS_2}$ 1733, 1240 (acetate) and 1717 cm^{-1} (C-21 ketone), NMR 7·97 (acetate), and 9·16 τ (C-18 + C-19—Me). (Found: C, 77·15; H, 9·85. $C_{23}H_{36}O_3$ requires: C, 77·65; H, 9·9%.)

3β-Hydroxy-5α,16α,17α-pentaran-21-one

A soln of 3β-hydroxy-5α,16α-pentar-17(20)-en-21-one (1·5 g) in EtOH (75 ml) was hydrogenated at NTP over pre-reduced Pd–charcoal (5%, 0·15 g); H uptake ceased after 10 min (105 ml, 1·05 eq.). After removal of the catalyst, the soln was evaporated to dryness and the residue was crystallized from CH_2Cl_2–acetone to give 3β-hydroxy-5α,16α,17α-pentaran-21-one (1·15 g) as prisms, m.p. 184°, $[\alpha]_D$ +138·1°; no UV absorption below 260 mμ, NMR 8·26 (OH), 9·16 (C-19—Me) and 9·23 τ (C-18—Me), ORD $[\phi]_{300}$ +11,900°; $[\phi]_{285}$ −11,300°; a, 232° (*c*, 0·025 in MeOH). (Found: C, 78·25; H, 10·55. $C_{23}H_{36}O_3 \cdot \frac{1}{2}H_2O$ requires: C, 78·15; H, 10·55%.)

The 3β-acetate (Ac_2O)–pyridine, 100° for 1 hr) formed laths from CH_2Cl_2–MeOH, m.p. 170–171°, $[\alpha]_D$ +113·1°, $\nu_{max}^{CCl_4:CS_2}$ 1733, 1245 (acetate) and 1717 cm^{-1} (C-21 ketone), NMR 7·98 (acetate) 9·16 (C-19—Me) and 9·25 τ (C-18—Me). (Found: C, 77·8; H, 10·2. $C_{25}H_{38}O_5$ requires: C, 77·65; H, 9·9%.)