Microbiological Hydroxylation. Part XVII.[1] C-19 Hydroxylation of 17-Oxo-5α-androstanes and 17-Oxo-3α,5-cyclo-5α-androstanes by the Fungus *Calonectria decora*

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The sequence of microbiological reactions involved in the 19-hydroxylation of 5α-androstan-17-one has been established. When a solution of 5α-androstan-17-one in dimethyl sulphoxide is incubated with *Calonectria decora*, the initial 1β,6α-dihydroxylation is followed by oxidation of the 1β-hydroxy-group and then by hydroxylation at C-19 to give 6α,19-dihydroxy-5α-androstane-1,17-dione in 36% yield. This compound is readily transformed (by chemical methods) into 5α,10β-estrane-1,6,17-trione.

C-19 hydroxylation occurs also with certain substituted 17-oxo-5α-androstanes and 17-oxo-3α,5-cyclo-5α-androstanes.

In the systematic study of the modification of 5α-androstane monoketones with the fungus *Calonectria decora* hydroxylation of the 17-ketone was found to lead cleanly to one product.[2] Thus, when an ethanolic solution of 5α-androstan-17-one was incubated with a culture of the micro-organism for 2 days, the 1β,6α-dihydroxy-17-ketone formed was almost free from contamination by other hydroxylation products. The more detailed investigation reported here was prompted by the observation that an increase in the incubation time, or the use of dimethyl sulphoxide for introducing the steroid, leads to more extensive hydroxylation. The formation of one of the products (see later) involves attack on the angular methyl group at position 10. Since C-19 hydroxylation is an uncommon microbiological reaction in general,[3] and unprecedented with *Calonectria decora*, a range of suitable substrates was studied in order to examine the scope of this hydroxylation.

Table 1 shows the substrates incubated with *C. decora* and the products formed. The Scheme portrays the hydroxylation of 5α-androstan-17-one, the parent substrate, and related chemical transformations. 1β,6α-Dihydroxy-5α-androstan-17-one (II) and the 6α-hydroxy-1,17-diketone (III), which were also used as substrates, were obtained by appropriate incubations of the 17-ketone (I). 5α-Androstane-1,17-dione (VIII) and the Δ^2-analogue were prepared from the commercially available 17β-hydroxy-3-ketone (V) as shown in the Scheme. Routes from 3β-hydroxyandrost-5-en-17-one to all but

[1] Part XVI, J. M. Evans, Sir Ewart R. H. Jones, G. D. Meakins, J. O. Miners, A. Pendlebury, and A. L. Wilkins, preceding paper.

[2] A. M. Bell, P. C. Cherry, I. M. Clark, W. A. Denny, Sir Ewart R. H. Jones, G. D. Meakins, and P. D. Woodgate, *J.C.S. Perkin I*, 1972, 1081.

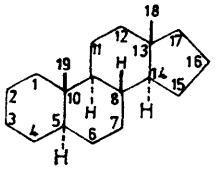
[3] *Inter alia*, W. Charney and H. L. Herzog, 'Microbial Transformations of Steroids,' Academic Press, New York, 1967, the most comprehensive of many reviews.

one of the 3,5-cyclo-substrates have been described elsewhere;[4-6] the last one, 6α,11α-dihydroxy-3α,5-cyclo-5α-androstan-17-one, was obtained by hydroxylating the 6α-hydroxy-3α,5-cyclo-17-ketone (Table 1).

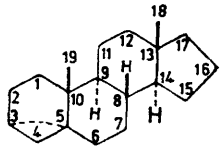
As usual, the structures of new compounds follow from chemical relationships and spectrometric examinations. With some of the oxygenated 3,5-cyclo-derivatives, calculation of the positions of the angular methyl groups' n.m.r. signals by using the standard shift values leads to unacceptable discrepancies. Moreover, it is not possible to ascribe invariable shift values to the 3α,5-cyclo-unit, and then to use the shift values computed for the 5α-androstane series, since the normally additive effects of oxygenated substituents at C-2 and C-6 are modified by the proximity of the cyclopropane ring. The simplest approach, developed by considering literature values for 2- and 6-substituted 3α,5-cyclocholestanes [7] and results of recent work,[6] is to treat the '3α,5-cyclo + nearby oxygen' system as a single unit whose shift values (Table 2) include the contributions of both components; for substituents in rings C and D the standard values [8,9] can then be used in calculating the positions of the 18-H and 19-H resonances. Table 3 lists the n.m.r. signals of compounds for which spectrometric data have not appeared in earlier publications: the arabic serial

TABLE 1

Hydroxylation of 17-oxo-5α-androstane and 17-oxo-3α,5-cyclo-5α-androstane derivatives by *Calonectria decora*



5α-Androstane



3α,5-Cyclo-5α-androstane

Substrates indicated by abbreviated names or symbols, *e.g.* 3α,5-cyclo–6α,11α–$(OH)_2$–17-CO represents 6α,11α-dihydroxy-3α,5-cyclo-5α-androstan-17-one. In the products column those oxygen functions introduced during incubations are in bold type. The entries under conditions refer to the use of ethanol (E) and dimethyl sulphoxide (D) as solvents for the substrate, and to the time of incubation (in days). The yields are calculated after making allowance for recovered starting material.

Substrate	Conditions	Substrate recovered	Main product(s)		Other product(s)	
17-CO	E1	75%	**1β,6α-** $(OH)_2$	15%		
	E2	32	**1β,6α-** $(OH)_2$	40	**1**-CO–**6α**, **19**-$(OH)_2$	3%
					1-CO–**6α**- (OH	2
	E4	11	**1β,6α-** $(OH)_2$	36	**1**-CO–**6α**, **19**-$(OH)_2$	8
					1-CO–**6α**- OH	1·5
	D4	5	**1**-CO–**6α**, **19**-$(OH)_2$	38	**1**-CO–**6α**- OH	1·5
					1β,6α- $(OH)_2$	16
17-CO–Δ^2	E2	12	**1**-CO–**6α**- OH	52	**1**-CO–**6α**, **19**-$(OH)_2$	6
	E4	5	**1**-CO–**6α**- OH	31	**1**-CO–**6α**, **19**-$(OH)_2$	18
	D4	0	**1**-CO–**6α**- OH	29	**1**-CO–**6α**, **19**-$(OH)_2$	24
1β,6α-$(OH)_2$–17-CO	D4	40	1-CO– **19**- OH	36	1-CO	29
	D4 *	9	1-CO– **19**- OH	56	1-CO	24
1,17-$(CO)_2$	E2	15	**6α**- OH	33	**6α**, **19**-$(OH)_2$	25
	D2	0	**6α**, **19**-$(OH)_2$	34	**6α**- OH	16
1,17-$(CO)_2$–Δ^2	D2	0	**6α**- OH	54	**6α**, **19**-$(OH)_2$	17
6α-OH–1,17-$(CO)_2$	E2	40	**19**- OH	26		
	D2	6	**19**- OH	29		
3α,5-cyclo–17-CO	E4	33	**2α,6β**- $(OH)_2$	26	**11α,15α**- $(OH)_2$	7
3α,5-cyclo–6α-OH–17-CO	D4	8	**11α**- OH	44	**19**- OH	5
					11α, **19**-$(OH)_2$	13
3α,5-cyclo–6β-OH–17-CO	E4	15	**11α**- OH	50		
			2α- OH	32		
3α,5-cyclo–6α,11α-$(OH)_2$–17-CO	D4	35	**19**- OH	24		
3α,5-cyclo–6,17-$(CO)_2$	D2	6	**11α,15α**- $(OH)_2$	12	**11α**- OH	8
					19- OH	8
					15α- OH	7
					2α- OH	4
	E4	5	**11α,15α**- $(OH)_2$	15	**15α**- OH	10
					11α- OH	9
					19- OH	9
					2α- OH	6

* Incubation in the presence of 5α-androstan-17-one as enzyme inducer.

[4] A. Kasal, V. Cerny, and F. Sorm, *Coll. Czech. Chem. Comm.*, 1965, **30**, 472.

[5] S. Julia, C. Neuville, and M. Davis, *Bull. Soc. chim. France*, 1960, 297.

[6] Sir Ewart R. H. Jones, G. D. Meakins, J. Pragnell, W. E. Müller, and A. L. Wilkins, *J.C.S. Perkin I*, 1974, 2376.

[7] V. Cerny, A. Kasal, and F. Sorm, *Coll. Czech. Chem. Comm.*, 1970, **35**, 1235.

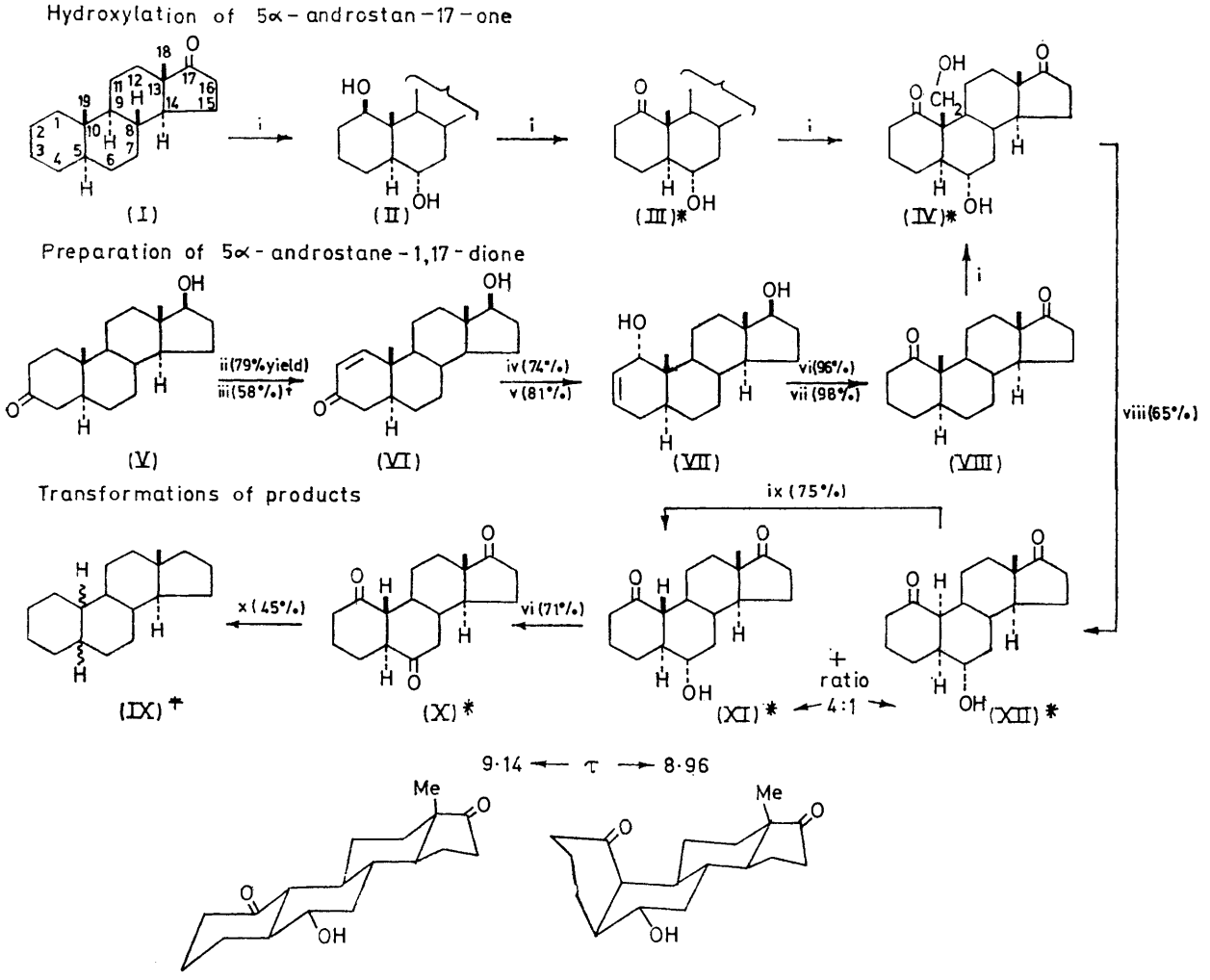
[8] J. E. Bridgeman, P. C. Cherry, A. S. Clegg, J. M. Evans, Sir Ewart R. H. Jones, A. Kasal, V. Kumar, G. D. Meakins, Y. Morisawa, E. E. Richards, and P. D. Woodgate, *J. Chem. Soc.* (*C*), 1969, 250.

[9] A. M. Bell, I. M. Clark, W. A. Denny, Sir Ewart R. H. Jones, G. D. Meakins, W. E. Müller, and E. E. Richards, *J.C.S. Perkin I*, 1973, 2131.

number sequence of steroids discussed earlier is used in this Table, which contains steroids nos. 790—829. The n.m.r. signals of new compounds appear in Table 3, and the other information required for their characterisation is given in Table 4. Since little of the work involves more than the routine operation of techniques fully described in earlier parts, most of the experimental details work establishes the details of this process for 5α-androstan-17-one (I) with *C. decora*: it involves the sequence (I) → (II) → (III) → (IV). This result, and the successful C-19 hydroxylation of 5α-androstane-1,17-dione (VIII), show that the presence of a 1-oxo-group (either present in the substrate, or introduced during the incubation) is essential for the attack on the

SCHEME Work on 17-oxo-5α-androstanes

References to known compounds are given in the Experimental section; new compounds are marked with an asterisk



Reagents: i, *C. decora* (see Table 1); ii, Br_2–AcOH; iii, Li_2CO_3–LiCl–DMF, reflux; iv, H_2O_2–NaOH; v, N_2H_4, heat; vi, H_2CrO_4–Me_2CO; vii, H_2–Pd; viii, BDN–DMF, reflux; ix, KOH–EtOH; x, Huang-Minlon reduction

† The other product was 17β-hydroxyandrost-4-en-3-one (31%). ‡ See Experimental section for configurations at positions 5 and 10.

are available only in supplementary Publication No.-SUP 21364 (12 pp., 1 microfiche).* However, the formation and transformations of 6α,19-dihydroxy-5α-androstane-1,17-dione (IV) are sufficiently novel to warrant description in the Experimental section.

C-19 hydroxylation is the key process in the biotransformation [10] of androgens into estrogens. The present angular methyl group of these substrates. 5α-Androst-2-en-17-one and the Δ^2-1,17-diketone undergo processes similar to those of the saturated analogues; as expected the olefinic bond of the Δ^2-17-ketone substrate facilitates oxidation of the 1β-hydroxy-group in the (presumed) initial dihydroxylated product.

* For details of Supplementary Publications see Notice to Authors No. 7 in *J.C.S. Perkin I*, 1974, Index issue.

[10] (*a*) J. E. Longchampt, C. Gual, M. Ehrenstein, and R. I. Dorfman, *Endocrinology*, 1960, **66**, 416; (*b*) M. Akhtar and S. J. M. Skinner, *Biochem. J.*, 1968, **109**, 318.

In contrast, the presence of a 3,5-cyclo-unit in the 17-ketone substrates leads to much less selective hydroxylations in which attack may occur at positions 2, 6, 11, 15, and 19. Significantly, no 1-hydroxylation is observed.

TABLE 2

The effect of substituents [$\Delta\tau_2(CDCl_3)$] on 19-H and 18-H signals. A positive $\Delta\tau_2$ value indicates a shift to higher field.

Substituent 5α,14α-Steroids	19-H	18-H
3α,5-cyclo	−0·14	−0·05
2α,6β-$(OH)_2$–3α,5-cyclo *	−0·30	−0·08
2α-OH–6-CO–3α,5-cyclo *	−0·23	−0·07
2,6-$(CO)_2$–3α,5-cyclo *†	−0·40	−0·09
6α-OH–3α,5-cyclo	−0·15	−0·04
6β-OH–3α,5-cyclo	−0·30	−0·05
6-CO–3α,5-cyclo	−0·24	−0·08

* Based on one or two examples only. † A similar value can be calculated in the cholestane series; see ref. 7.

(It was considered necessary to support the structures of the products, as deduced from their spectra, by chemical evidence. Accordingly, the major product from 3α,5-cyclo-5α-androstan-17-one, formulated as a 2,6-dihydroxy-compound, was oxidised and then hydrogenated to the known 5α-androstane-2,6,17-trione.) It may be that the altered geometry of the substrate brings the enzyme sites normally responsible for 1,6-dihydroxylation into contact with the 2- and 6-positions, but in a manner less favourable for attack, and this would allow other hydroxylations (at the 11- and 15-positions) to compete or supervene. In general the extent of 19-hydroxylation is much reduced with the 3,5-cyclo-androstanes. The best yield is obtained with an 11α-hydroxy-17-ketone; in such circumstances the 11α-hydroxy-group appears to facilitate substitution of the angular C-10 methyl group.

With the 6α-hydroxy-1,17-dioxo-5α-estranes [obtained, see Scheme, by the reversed aldol reaction of the 19-hydroxy-1-oxo-functionality of the dihydroxy-diketone (IV)] the structures assigned from the expected greater stability of the 10β *H*-isomer (XI) were confirmed by marked deshielding of the 18-protons by the 1-oxo-group in 10α *H*-isomer (XII). Mild oxidation of the 10β-compound (XI) gave a trione for which the 5α,10β-structure (X) was established by n.m.r. solvent shift studies. On treatment with alkali this trione appeared to be partially converted into an isomer (presumably [11] the 5β,10β-compound, which would represent the more stable arrangement of a 5ξ,10ξ-1,6-dioxoestrane system). Although this isomerisation was not studied in detail, its occurrence to some extent during the Huang-Minlon reduction of the triketone (X) is probable; the constants of the resulting hydrocarbon material are consistent [12] with its being a mixture of 5α- and 5β-estrane.

EXPERIMENTAL

For general directions see refs. 2, 6, and 13. For the n.m.r. signals and the other constants of new compounds, see Tables 3 and 4. The constants (m.p., $[\alpha]_D$) of known compounds are not given if the values found here correspond closely with those in the literature references cited. *Cd* refers to *Calonectria decora*.

6α,19-*Dihydroxy*-5α-*androstane*-1,17-*dione* (IV).—*Preparation*. Incubation of 5α-androstan-17-one [2] (I) (no. 20) * with *Cd*; 4·0 g in Me_2SO (400 ml), 100 flasks, medium B, 4d, extraction I ⟶ 1·05 g, mycelial extract and 3·9 g broth extract. Chromat. of the mycelial extract on Al_2O_3 (5% deactivated, 50 g) and elution with petrol–EtOAc (4 : 1) gave s.m. (200 mg). Chromat. of the broth extract on Al_2O_3 (5% deactivated, 150 g) and elution with petrol–EtOAc (2 : 1) gave material (120 mg) separated by p.l.c. [3 small plates, CH_2Cl_2-Me_2CO–EtOH (16 : 2 : 1)] into 1β,6α-dihydroxy-5α-androstan-17-one (II) (no. 235)* (68 mg), and 6α-*hydroxy*-5α-*androstane*-1,17-*dione* (III) (no. 801) (68 mg), $\nu_{max.}$ 3600, 1745, and 1714 cm^{-1}. Elution with petrol–EtOAc (1 : 1) gave further 1β,6α-dihydroxy-5α-androstan-17-one (I) (606 mg). Elution with EtOAc gave 6α,19-*dihydroxy*-5α-*androstane*-1,17-*dione* (IV) (no. 804) (1·68 g), $\nu_{max.}$ (Nujol) 3440, 1738, and 1690 cm^{-1}.

TABLE 3

N.m.r. signals

The results, presented in the form used earlier,[6] were obtained by examining solutions in $CDCl_3$ at 100 MHz

No.	Compound		τ_2	τ_2 (calc.)			>CH–OH *etc.*
	5α-Androstanes						
790	5α-Androst-2-en-17-one	19	9·22	9·21	H-2	4·42	s
		18	9·13	9·12	H-3		
791	5α-Androstane-1,17-dione	19	8·83	8·82			
		18	9·14	9·12			
792	5α-Androst-2-ene-1,17-dione	19	8·92	8·93	H-2	4·15	d (10·5)
		18	9·12	9·10	H-3	3·25	*δ* (10·5, 6, 2)
793	5α-Androst-2-ene-1,6,17-trione	19	8·92	8·91	H-2	4·15	d (10)
		18	9·10	9·07	H-3	3·24	*δ* (10, 6, 2)
794	5β-Androst-2-ene-1,6,17-trione	19	8·90	8·90	H-2	3·97	d (10)
		18	9·12	9·12	H-3	3·19	m (18)
795	17,17-Ethylenedioxyandrost-5-en-3β-ol	19	8·97	8·97	H-3	6·51	m (21)
					H-6	4·52	d (5)
		18	9·13	9·13	Acetal	6·14	s
796	17,17-Ethylenedioxyandrost-5-en-3β-yl toluene-4-sulphonate	19	9·00	9·00	H-3	5·54	7 (10, 10, 5, 5)
					H-6	4·54	d (5)
		18	9·14	9·14			
797	17-Oxo-5α-androstan-3β-yl toluene-4-sulphonate	19	9·20	9·19	H-3	5·60	7 (10, 10, 5, 5)
		18	9·16	9·14			
798	2α-Bromo-17β-hydroxy-5α-androstan-3-one	19	8·90		H-2	5·24	*4* (13, 6)
		18	9·24		H-17	6·35	t (8)
799	1α,2α-Epoxy-17β-hydroxy-5α-androstan-3-one	19	9·10	9·12	H-1	6·48	d (4)
					H-2	6·88	d (4)
		18	9·23	9·24	H-17	6·33	t (8)
800	17β-Hydroxy-5α-androst-1-en-3-one	19	8·98	8·99	H-1	4·10	d (10)
					H-2	2·88	d (10)
		18	9·24	9·24	H-17	6·34	t (8)
801	6α-Hydroxy-5α-androstane-1,17-dione	19	8·82	8·79	H-6	6·42	*6* (11,11,4)
		18	9·13	9·12			
802	6α-Hydroxy-5α-androst-2-ene-1,17-dione	19	8·91	8·90	H-6	6·35	*6* (11, 11, 4)
					H-2	4·15	*4* (10, 2)
		18	9·11	9·10	H-3	3·22	*δ* (10, 6, 2)
803	5α-Androst-2-ene-1α,17β-diol	19	9·28	9·28	H-1	6·28	*A*1 (10)
		18	9·26	9·25	H-17	6·48	t (8)
804	6α,19-Dihydroxy-5α-androstane-1,17-dione	18	9·10		H-6	6·54	*6* (11, 11, 4)
					H-19	5·72, 6·04	*4* 'AB (12)
805	6α,19-Diacetoxy-5α-androstane-1,17-dione	18	9·12		H-6	5·24	*6* (10, 10, 5)
					H-19	5·45, 5·23	*4* ' AB ' (11)
806	6α,19-Dihydroxy-5α-androst-2-ene-1,17-dione	18	9·09		H-6	6·10	m (14)
					H-19		
					H-2	4·10	d (10)
					H-3	3·13	m (16)
807	6α,19-Diacetoxy-5α-androst-2-ene-1,17-dione	18	9·10		H-6	5·02	*6* (11, 11, 4)
					H-19	5·59, 5·75	*4* ' AB ' (11)
					H-2	4·07	d (10)
					H-3	3·20	*δ* (10, 6, 2)

[11] J. E. Bridgeman, P. C. Cherry, W. R. T. Cottrell, Sir Ewart R. H. Jones, P. W. Le Quesne, and G. D. Meakins, *Chem. Comm.*, 1966, 561.

[12] R. E. Counsell, *J. Medicin. Chem.*, 1966, **9**, 263.

[13] J. W. Blunt, I. M. Clark, J. M. Evans, Sir Ewart R. H. Jones, G. D. Meakins, and J. T. Pinhey, *J. Chem. Soc.* (*C*), 1971, 1136.

TABLE 3 (*Continued*)

No.	Compound		τ_2	τ_2 (calc.)		>CH–OH *etc.*	
	3α,5-Cyclo-5α-androstanes						
808	3α,5-Cyclo-5α-androstan-17-one	19	9·08	9·06			
		18	9·10	9·09			
809	17,17-Ethylenedioxy-3α,5-cyclo-5α-androstan-6-one	19	8·97	8·98	Acetal	6·15	s
		18	9·09	9·09			
809	17,17-Ethylenedioxy-3α,5-cyclo-5α-androstan-6-one	19	8·97	8·98	Acetal	6·15	s
		18	9·09	9·09			
810	3α,5-Cyclo-5α-androstane-2,6,17-trione	19	8·80	8·80			
		18	9·05	9·05			
811	6α-Hydroxy-3α,5-cyclo-5α-androstan-17-one	19	9·04	9·05	H-6	6·06	*4* (10, 5)
		18	9·10	9·10			
812	17,17-Ethylenedioxy-3α,5-cyclo-5α-androstan-6α-ol	19	9·07	9·07	H-6	6·06	*4* (10, 5)
		18	9·12	9·13	Acetal	6·15	s
813	17,17-Ethylenedioxy-3α,5-cyclo-5α-androstan-6β-ol	19	8·94	8·92	H-6	6·65	t (3)
		18	9·10	9·12	Acetal	6·14	s
814	2α-Hydroxy-3α,5-cyclo-5α-androstane-6,17-dione	19	8·97	8·97	H-2	5·73	d (5)
		18	9·07	9·07			
815	11α-Hydroxy-3α,5-cyclo-5α-androstane-6,17-dione	19	8·83	8·84	H-11	5·90	*6* (10, 10, 5)
		18	9·02	9·03			
816	6,17-Dioxo-3α,5-cyclo-5α-androstan-11α-yl acetate	19	8·89	8·88	H-11	4·66	*6* (10, 10, 5)
		18	8·98	8·99			
817	15α-Hydroxy-3α,5-cyclo-5α-androstane-6,17-dione	19	8·95	8·95	H-15	5·65	q (8)
		18	9·05	9·03			
818	19-Hydroxy-3α,5-cyclo-5α-androstane-6,17-dione	18	9·06		H-19	{6·15} {6·63}	*4* 'AB' (12)
819	2α,6β-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	19	8·91	8·91	H-2	5·78	d (5)
		18	9·06	9·06	H-6	6·60	t (3)
820	6α,11α-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	19	8·91	8·93	H-6	} 6·10	m (22)
		18	9·08	9·07	H-11		
821	6α,19-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	18	9·06		H-19	{6·15} {6·44}	*4* 'AB' (12)
822	6β,11α-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	19	8·76	8·78	H-6	6·70	t (3)
		18	9·08	9·06	H-11	5·85	*6* (10, 10, 5)
823	11α,15α-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	19	8·92	8·93	H-11	6·05	*6* (10, 10, 5)
		18	9·04	9·03	H-15	5·60	q (9)
824	11α,15α-Dihydroxy-3α,5-cyclo-5α-androstane-6,17-dione *	19	8·92		H-11	6·24	*6* (10, 10, 5)
		18	9·15		H-15	5·82	q (8)
825	[6α,11α,19-Trihydroxy-3α,5-cyclo-5α-androstan-17-one]						
826	6α,11α,19-Triacetoxy-3α,5-cyclo-5α-androstan-17-one	18	8·99		H-6	} 4·90	m (23)
					H-11		
					H-19	{6·05} {5·80}	*4* 'AB' (12)
	5α-Estranes						
827	5α-Estrane-1,6,17-trione	18	9·11	9·10 †			
828	6α-Hydroxy-5α-estrane-1,17-dione	18	9·14	9·09 †	H-6	6·55	*6* (10, 10, 4)
829	6α-Hydroxy-5α-10α-estrane-1,17-dione	18	8·96		H-6	6·45	*6* (11, 11, 4)

* In $(CD_3)_2SO$. † Calc. from values in 5α-androstane series.

[a] Ref. 9.

Transformations. A solution of 6α,19-dihydroxy-5α-androstane-1,17-dione (IV) (no. 804) (180 mg) in DMF (20 ml)–DBN (1,5-diazabicyclo[4.3.0]non-5-ene) (0·5 ml) was heated under reflux for 6 h. Work-up gave material (135 mg) separated by p.l.c. [1 large plate, 4 × Et_2O] into 6α-*hydroxy*-5α,10α-*estrane*-1,17-*dione* (XII) (no. 829) (21 mg), $\nu_{max.}$ 3625, 1743, and 1713 cm^{-1}; and 6α-*hydroxy*-5α-*estrane*-1,17-*dione* (XI) (no. 828) (85 mg), $\nu_{max.}$ 3630, 1743, and 1716 cm^{-1}.

A solution of the 5α,10α-hydroxy-diketone (XII) (12 mg) and KOH (5 mg) in EtOH (9 ml)–H_2O (1 ml) was heated under reflux for 2 h. Work-up gave the 5α,10β-hydroxy-diketone (XI) (9 mg).

Oxidation of the 5α,10β-hydroxy-diketone (XI) (30 mg) with 8N-H_2CrO_4 gave material purified by p.l.c. [1 small plate, 2 × Et_2O] to give 5α-*estrane*-1,6,17-*trione* (X) (no. 827) (21 mg), $\nu_{max.}$ 1712 and 1243 cm^{-1}; τ_1 9·16, τ_2 9·11, τ_3 9·48 (H-18); Δ_1^3 +0·32, Δ_2^3 +0·37 (calc. Δ_1^3 +0·36, Δ_2^3 +0·40 from values in androstane series [8,11]).

Huang-Minlon reduction of the foregoing 5α-trione (XI) (16 mg) gave material (10 mg), which after distillation *in vacuo* (sublimation tube) at 60° and 5 mmHg, had *m/e* 258 (M^+), $[\alpha]_D$ +17° (*c* 0·1) (lit.,[12] $[\alpha]_D$ +20° for 5α-estrane, $[\alpha]_D$ +15° for 5β-estrane, $[\alpha]_D$ −15·5° for 5α,10α-estrane), τ 9·29 (18-H).

TABLE 4

Characterisation of new compounds

Compound	M.p. (°C) (solvent for crystallisation)	$[\alpha]_D$ (°) (*c*) *	Analyses (%)	C	H
5α-Androst-2-ene-1,6,17-trione	144—146 (Me_2CO–hexane)	+189 (1·05)	Found	75·9	8·1
			$C_{19}H_{24}O_3$ req.	76·0	8·0
5β-Androst-2-ene-1,6,17-trione	186—188 (Me₂CO–hexane)	+140 (0·7)	Found	76·1	8·2
			$C_{19}H_{24}O_3$ req.	76·0	8·0
6α-Hydroxy-5α-androstane-1,17-dione	239—240 (Me₂CO–hexane)	+210 (0·5)	Found	75·2	9·3
			$C_{19}H_{28}O_3$ req.	75·0	9·2
6α-Hydroxy-5α-androst-2-ene-1,17-dione	242—244 (Me_2CO–hexane)	+225 (0·65)	Found	75·3	8·7
			$C_{19}H_{26}O_3$ req.	75·5	8·6
6α,19-Dihydroxy-5α-androstane-1,17-dione	227—229 (EtOAc)	+195 (1·0)	Found	71·2	8·8
			$C_{19}H_{28}O_4$ req.	71·2	8·8
6α,19-Diacetoxy-5α-androstane-1,17-dione	174—176 (MeOH–H_2O)	+160 (0·9)	Found	68·3	8·0
			$C_{23}H_{32}O_6$ req.	68·3	8·0
6α,19-Dihydroxy-5α-androst-2-ene-1,17-dione	185—187 (Me_2CO–hexane)	+205 (0·4)	Found	71·9	8·1
			$C_{19}H_{26}O_4$ req.	71·7	8·2
6α,19-Diacetoxy-5α-androst-2-ene-1,17-dione	158—160 (Me_2CO–hexane)	+185 (0·8)	Found	68·5	7·7
			$C_{23}H_{30}O_6$ req.	68·85	7·5
3α,5-Cyclo-5α-androstane-2,6,17-trione	231—233·5 (Me_2CO–hexane)	+28 (0·4)	Found	76·2	8·1
			$C_{19}H_{24}O_3$ req.	76·0	8·05
2α-Hydroxy-3α,5-cyclo-5α-androstane-6,17-dione	213—214 (Me_2CO–hexane)	+107 (1·0)	Found	75·7	8·6
			$C_{19}H_{28}O_3$ req.	75·45	8·7
11α-Hydroxy-3α,5-cyclo-5α-androstane-6,17-dione	152—154 (Me_2CO–hexane)	+91 (1·0)	Found	75·5	8·7
			$C_{19}H_{28}O_3$ req.	75·45	8·7
6,17-Dioxo-3α,5-cyclo-5α-androstan-11α-yl acetate	210—211 (MeOH)	+15 (0·1)	Found	73·1	8·2
			$C_{21}H_{28}O_4$ req.	73·2	8·2
15α-Hydroxy-3α,5-cyclo-5α-androstane-6,17-dione	214—217 (Me_2CO–hexane)	+121 (0·1)	Found	75·5	8·75
			$C_{19}H_{28}O_3$ req.	74·45	8·7
19-Hydroxy-3α,5-cyclo-5α-androstane-6,17-dione	173—175 (Me_2CO–hexane)	+135 (1·0)	Found	75·7	8·6
			$C_{19}H_{28}O_3$ req.	75·45	8·7
2α,6β-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	185—189 (C_6H_6–hexane)	+113 (0·5)	Found	74·7	9·2
			$C_{19}H_{28}O_3$ req.	75·0	9·3
6α,11α-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	181—182 (Me_2CO–hexane)	+107 (0·45)	Found	75·1	9·3
			$C_{19}H_{28}O_3$ req.	75·0	9·3
					9·2
6α,19-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	178—180 (Me_2CO–hexane)	+105 (0·65)	Found	74·8	
			$C_{19}H_{28}O_3$ req.	75·0	9·3
6β,11α-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	201—203 (Me_2CO)	+76 (0·3)	Found	75·0	9·1
			$C_{19}H_{28}O_3$ req.	75·0	9·3
11α,15α-Dihydroxy-3α,5-cyclo-5α-androstan-17-one	232—234 (Me_2CO)	+172 (0·5)	Found	75·2	9·4
			$C_{19}H_{28}O_3$ req.	75·0	9·3
11α,15α-Dihydroxy-3α,5-cyclo-5α-androstane-6,17-dione	285—290 (Me_2CO)	+95 (0·7)	Found	71·7	8·2
			$C_{19}H_{26}O_4$ req.	71·7	8·2
6α,11α,19-Triacetoxy-3α,5-cyclo-5α-androstan-17-one	165—168 (Me_2CO–hexane)	+25 (0·25)	Found	67·5	7·5
			$C_{25}H_{34}O_7$ req.	67·3	7·6
5α-Estrane-1,6,17-trione	189—191 (Me_2CO–hexane)	+101 (0·9)	Found	75·1	8·2
			$C_{18}H_{24}O_3$ req.	75·0	8·3
6α-Hydroxy-5α-estrane-1,17-dione	136—138 (Me_2CO–hexane)	+143 (1·2)	Found	74·3	8·9
			$C_{18}H_{28}O_3$ req.	74·5	8·95
6α-Hydroxy-5α,10α-estrane-1,17-dione	201—204 (Me_2CO–hexane)	+80 (0·8)	Found	74·6	9·1
			$C_{18}H_{28}O_3$ req.	74·5	8·95

* In $CHCl_3$.

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