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SYNTHESIS AND CONFORMATIONAL ANALYSIS OF A-HOMO-B-NOR AND A-NOR-B-HOMO STEROIDS[1]

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Abstract—A stereospecific rearrangement of a series of 1,2-*cis*-diol monotosylates is described. The 5-hydroxy-6-tosyloxy derivatives, **2**, lead to the A-homo-B-norketones **3** and **4** and the 5-hydroxy-4-tosyloxy derivatives **11**, **12** and **28** to the A-nor-B-homoketones **13**, **14** and **29**. Rearrangement of 3-acetoxy-5-hydroxy-4-tosyloxy derivatives **31** however, results in the 3-aldehydo-A-nor-steroids **32**.

ORD and NMR data are reported and used to assign preferred conformations to the 7-membered rings of the rearranged keto-steroids **3**, **4**, **13** and **14**.

DIOL monotosylates may undergo pinacolic type rearrangements resulting in formation of carbonyl derivatives.[2]

Mono-tosylates of the 5,6- and 4,5-steroidal diols, were found to rearrange to compounds possessing the perhydroazulene skeleton: the former compounds gave A-homo-B-nor, and the latter the A-nor-B-homo derivatives. The C—C bond which is *trans* coplanar to the leaving group is most likely to migrate and a stereospecific rearrangement with retention of configuration at the new ring junction was expected.[2] The mono-tosylates of these α-diols will yield ketones having a β-hydrogen, and those of the β-diols, ketones having α-hydrogen at the new ring junction.

A-Homo-B-nor-steroids

This system was synthesized in both the cholestane and the androstane series by rearrangement of the 5α-hydroxy-6α-tosyloxy-derivatives **2b**, and **2d**. In the cholestane series, the 5α,6α-diol **2a**,[3] obtained by osmium tetroxide hydroxylation of Δ^5-cholestene **1a**, was tosylated to give **2b**. Treatment of **2b** with potassium t-butoxide in t-butanol at room temperature, or in dimethylformamide in the presence of calcium carbonate at higher temperature, gave the 6β-ketone **3a**. This ketone was converted by acid to an equilibrium mixture of both **3a** and the 6α-ketone **4a** in ca. 4:1 ratio. A similar equilibrium mixture was obtained when the tosylate **2b** was chromatographed on acid-washed alumina.

In the androstane series, the corresponding 17β-benzyloxy-5α,6α-diol **2c**, was prepared from the olefin **1b** by osmium tetroxide hydroxylation. The 6α-tosylate **2d** rearranged on heating in dimethylformamide in the presence of calcium carbonate to give the 6β-ketone **3c**. Acid hydrolysis of the latter led to a crystalline mixture of the two keto-alcohols **3b** and **4b** which could not be separated. The NMR spectrum of the mixture showed it to contain the two keto-alcohols in a ratio corresponding roughly to that of the equilibrium mixture of the two respective ketones **3a** and **4a**.

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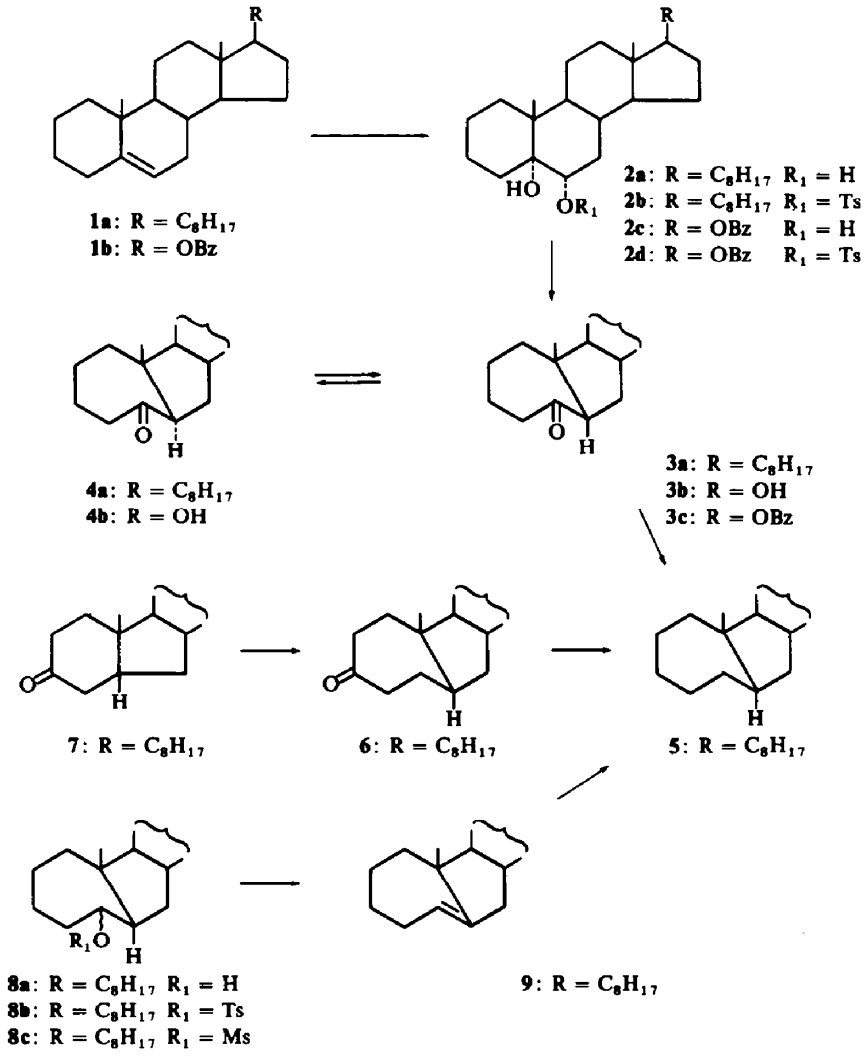


CHART I

Heating of the tosylate **2d** with potassium t-butoxide in t-butanol also gave a mixture of the two ketones **3b** and **4d** in the same ratio.

The structure of the thermodynamically more stable ketone **3a** was proved through its conversion by a Wolff–Kishner reduction to the hydrocarbon **5**. This hydrocarbon was synthesized independently from the known B-norketone **7**,[4] by enlargement of ring A with diazomethane to the A-homo-B-nor-ketone **6**. Wolff-Kishner reduction converted **6** to the hydrocarbon **5**, identical with the Wolff-Kishner product of **3a**. An identical hydrocarbon **5** was also obtained by catalytical-hydrogenation of the olefin **9**, the product of elimination of the tosylate **8b** or the mesylate **8c**.

A-*Nor*-B-*homo*-steroids

The starting materials for this system in the cholestane series were the 4β-tosyloxy-5β-hydroxy-cholestane **11a**,[5]† and the 4α-tosyloxy-5α-hydroxy-cholestane **12a**.[5]† Treatment of **11a** with potassium t-butoxide in t-butanol at room temperature, or heating in dimethylformamide in the presence of calcium carbonate, gave in almost quantitative yield the 4α-ketone **13a**.‡ On the other hand the rearrangement of the 4α-tosyloxy-5α-hydroxy-cholestane **12a** under similar conditions led to 4β-ketone **14a**.‡

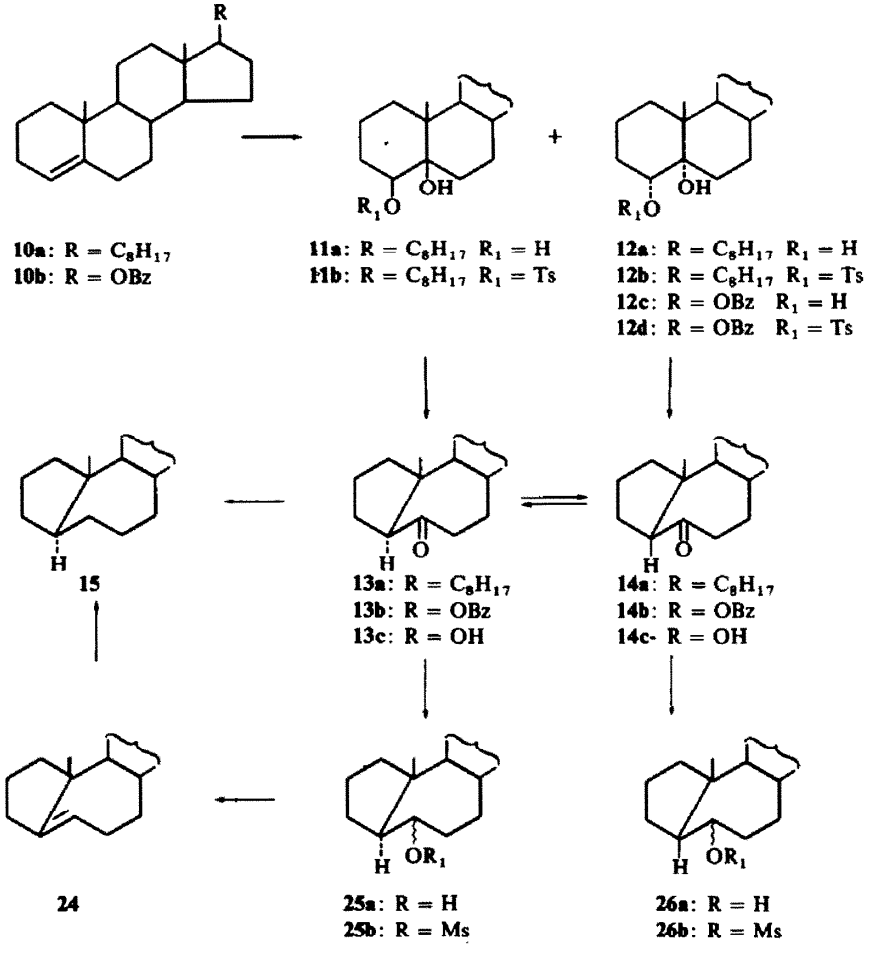
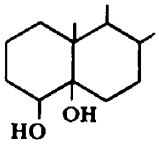
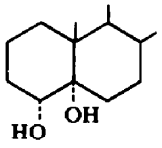
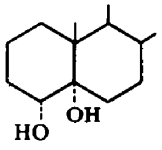
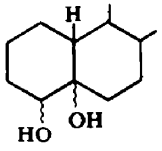
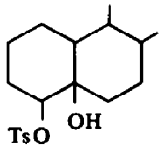
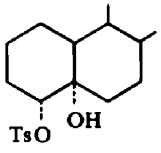
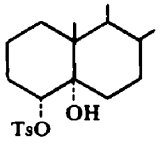
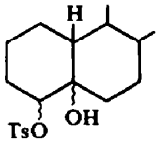


CHART II

† We are indebted to Dr. J. Kalvoda, "Ciba A.G.", Switzerland, for pointing out to us that the 4,5-dihydroxy and 4-tosyloxy-5-hydroxycholestanes previously reported by us[1] as being the 4α,5α-derivatives were in fact the 4β,5β-derivatives. Comparison with the authentic samples by Dr. J. Kalvoda (m.m.p. and IR) proved these identities.

‡ The configuration of C-4 of **13a** and **14a** was erroneously reported by us[1] to be 4β and 4α respectively.

TABLE 1. NMR DATA FOR THE *cis* 4,5-DIHYDROXYSTEROIDS AND THE *cis*-4-TOSYLOXY-5-HYDROXYSTEROIDS **11, 12** AND **28.**

Compound		Protons at[a] C_{18}	C_{19}	C_4
	**11a**	0·61	0·95	4·08
	**12a**	0·66	0·92	3·66
	**12c**	0·95	0·93	3·70
	**28a**	0·78		3·83
	**11b**	0·61	0·93	5·08
	**12b**	0·61	0·90	4·66
	**12d**	0·94	0·90	4·66
	**28b**	0·76		4·78

[a] The chemical shifts are given in δ (ppm).

Both ketones **13a** and **14a** were equilibrated after heating at 100° in acid solution, their ratio in the equilibrium mixture being 4:1. A similar ratio of **13a** and **14a** was obtained after either was heated with potassium t-butoxide in t-butanol.

A corresponding 4α-tosyloxy-5α-alcohol **12d** id the androstane series was synthesized from the Δ^4-olefin **10b** by hydroxylation with osmium tetroxide to the α-cis diol **12c** and subsequent tosylation. The configuration at C-4 in the α-*cis* diol **12c** and in its tosylate **12d** was assigned by the comparison of their NMR spectra with those of the 4α,5α-cholestane-derivatives **12a** and **12b** and of 4β,5β-cholestane derivatives **11a** and **11b**. In both compounds of the androstane series, **12c** and **12d** the C-4 protons have a similar chemical shift as the C-4 protons in the respective 4α,5α-derivatives, **12a** and **12b** of the cholestane series and therefore possess also the 4α,5α-configuration.

Heating of the tosylate **12d** in dimethylformamide in the presence of calcium carbonate yielded the less stable 4β-keto-benzoate **14b**. When the rearrangement of **12d** was effected by heating with potassium t-butoxide in t-butanol, a 4:1 mixture of 4α and 4β-keto alcohols **13c** and **14c** was obtained. Each of the alcohols **13c** and **14c** was converted to the corresponding benzoates **13b** and **14b**. Furthermore, each of the two compounds upon heating with acid was equilibrated to a similar mixture of **13b** and **14b**. The A-nor-B-homo-ketone **13c** obtained recently by Wehrli *et al.*[6] from 17β-acetoxy-A-nor-B-homo-3,5-diketo-androstane, was found to be identical with the ketone described by us. An independent proof of its structure and configuration at C-10 (but not C-4) is given by these workers.

Proof of the structure and configuration at C-4 in the A-nor-B-homo-ketone **13a** was obtained by an independent synthesis of the hydrocarbon **15**. The starting material

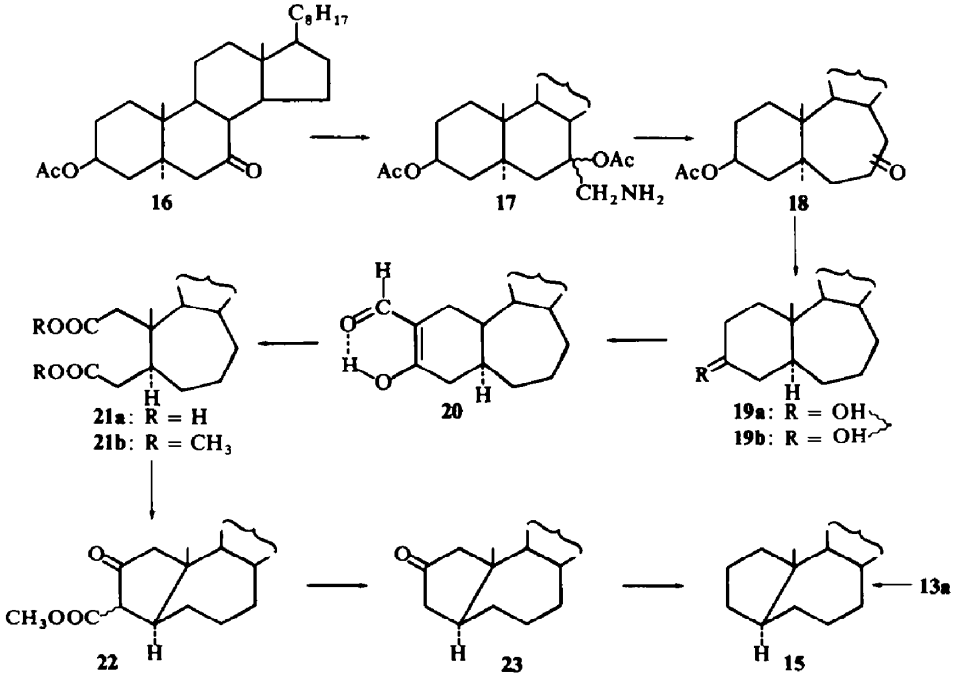
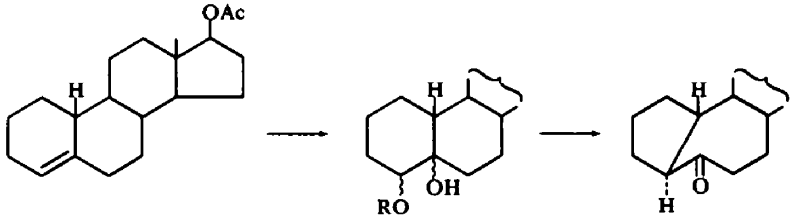


CHART III

for the synthesis outlined in Chart III was the 3β-acetoxy-7-ketone **16**.[17] Ring B was first enlarged to the 7-membered homologue followed by contraction of ring A to the 5-membered one. The resulting A-nor-B-homo-2-ketone **23**, was transformed to the hydrocarbon **15** which was found to be identical with the Wolff–Kishner reduction product of the 4α-ketone **13a**.

The epimeric ketones **13a** and **14a** were reduced with LAH to the respective alcohols **25a** and **26a**. The corresponding mesylates **25b** and **26b** were further converted with LAH in THF to the olefin **24**. The latter, on catalytic hydrogenation gave the hydrocarbon **15**. It should be noted that hydrogenation of the Δ^3-A-homo-B-nor olefin **9** proceeded from the β-side of the steroidal molecule, while hydrogenation of the Δ^4-A-nor-B-homo olefin **24** proceeded from the α-side.

The A-nor-B-homo-ketone **29a** in the estrane series was prepared from 17β-acetoxy-Δ^4-estrene[7] **27** by an analogous reaction sequence: hydroxylation of **27** with osmium tetroxide gave the 4,5-diol, **28a** which was subsequently tosylated to give **28b**. The configuration at C-4 and C-5 in **28** was not established. Comparison of the chemical shift of the C-4 protons **28a** and **28b** with those of the respective C-19 Me derivatives in both 4β,5β and 4α,5α series (Table 1) does not serve as conclusive



27 **28a**: R = H **28b**: R = Ts **29a** **29b**: (17βOH)

CHART IV

proof of the configuration at C-4. The rearrangement of the tosylate **28b** in DMF in the presence of calcium carbonate, or in t-butanol in the presence of potassium t-butoxide resulted in formation of the ketone **29a**. This ketone did not epimerize at C-4 when heated with acids or bases. We assigned to it the 4α-configuration by analogy to the C-19 Me series, in which the 4α epimer is the more stable one. A Cotton effect was observed in the 19-nor derivative **29b** having similar positive sign and similar amplitude to the 4α ketones **13a** and **13b** (Table 4, Fig. 2) thereby supporting this assignment. An identical ketone **29b**, was synthesized by a different route by Muller and Martel† starting from 17β-acetoxy-$\Delta^{5(10)}$-estren-3-one.

A-Nor-aldehydes

With the aim of synthesizing A-nor-B-homo steroids possessing an additional oxygen function at C-3 we attempted to rearrange the 3-acetoxy-4-tosyloxy-5-hydroxy-derivatives in both the androstane and estrane series.

Suitable derivatives **31b** and **31d** were prepared by reacting the 3β-acetoxy-Δ^4-olefins **30a** and **30b** with osmium tetroxide followed by treatment with tosyl chloride in pyridine. The configuration at C-4 and C-5 in the two *cis*-diols **31a** and **31c** and

† We are indebted to Muller and Martel[8] for a sample of **29b**.

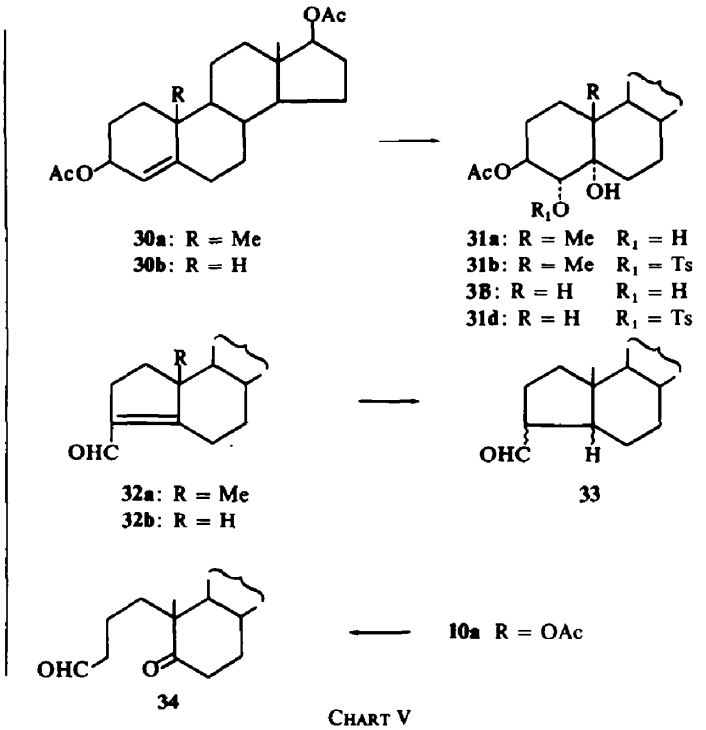
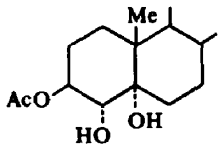
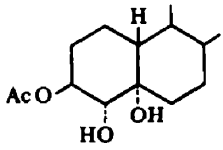
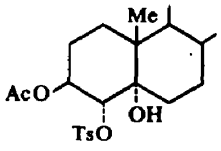
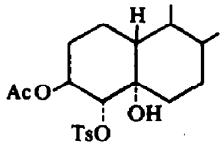


CHART V

the two tosylates **31b** and **31d** was suggested by their NMR spectra (Table 2). The signals assigned to the C-4 proton in the four compounds appeared as doublets with $J = 9{\cdot}5$ c/s. This coupling value indicates an axial axial coupling of the C-4 proton with the neighbouring C-3 proton. In the alternative product which might have arisen from a β-side attack of osmium tetroxide on the Δ^4-olefins **30a**, the protons at C-3 are equatorial and the coupling value with the C-4 protons should have been smaller. The comparatively high field chemical shift values obtained for the acetoxy protons at C-3 in **31b** and **31d** corroborate this assignment. The shielding effect of the tosyl chromophore on the acetoxy protons at C-3 is more likely to occur when both groups are equatorial rather than in the alternate structure in which the acetoxy group is axial. Both tosylates **31b** and **31d** failed to give the desired A-nor-B-homo derivatives when exposed to similar conditions as compounds lacking the acetoxy function. However, methanolic potassium hydroxide at room temperature converted both tosylates **31b** and **31d** to the two unsaturated aldehydes **32a** (17β-OH) and **32b** (17β-OH) respectively. Their structure was indicated by the analytical and spectral data. The aldehyde **32a** was also synthesized independently from the Δ^4-olefin **10** (17β-OAc) by ozonolysis to the keto-aldehyde **34**, followed by ring closure with base and reacetylation.

Catalytic reduction of the unsaturated aldehyde **32a** with Pd–C resulted in the saturated aldehyde **33**, characterized as the semicarbazone.

TABLE 2. NMR DATA FOR THE 3-ACETOXY-4,5-DIHYDROXYSTEROIDS AND THE 3-ACETOXY-4-TOSYLOXY-5-HYDROXYSTEROIDS 31.

Compound		Protons at [a] C_{18}	C_{19}	C_4	C_{17} (OAc)	C_3 (OAc)
	**31a**	0·80	1·00	3·58d $J = 9·5$	2·03	2·08
	**31c**	0·80		3·33d $J = 9·5$	2·03	2·07
	**31b**	0·78	1·03	4·93d $J = 9·5$	2·03	1·65
	**31d**	0·78		4·50d $J = 9·5$	2·01	1·64

[a] The chemical shifts are given in δ (ppm), coupling constants in c/s.

IR *and* UV *measurements*

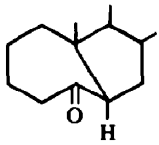
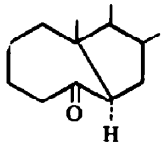
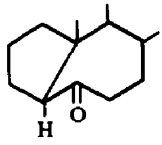
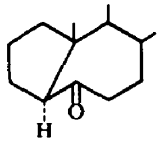
The CO stretching vibrations of the four types of ketone **3**, **4**, **13**, and **14** appeared between 5·86–5·87 μ as expected for 7-membered ring ketones.[9] However, small differences were observed between ketones having A/B *trans* and those having A/B *cis* junctions, the former absorbing at somewhat lower frequencies than the latter (Table 3).

The n → π* transitions of the CO functions in the 7-membered ketones appeared at values similar to those of 6-membered ketones. Both the A/B *trans* ketones **4** and **13** and the A/B *cis* ketone **14** absorbed in dioxan at 288–289 mμ. The only exception was the A-nor-B-homo-4β-ketone **3** which absorbed at a lower wave length, at λ_{max} 283 mμ (Table 3).

ORD *measurements*

The ORD curves of the two epimeric A-homo-B-nor-keto-steroids **3a** and **4a** exhibit Cotton effects of similar magnitude but of opposite signs, the former being

TABLE 3. IR AND UV DATA FOR THE A-HOMO-B-NOR AND A-NOR-B-HOMOSTEROIDS 3, 4, 13 AND 14.

Compound		IR(μ)[a] λ_{μ}^{KBr}	UV (mμ)[b] $\lambda_{max}(\varepsilon)$
	**3a**	5·865	289 (29)
	**4a**	5·868	289 (30)
	**14a**	5·865	283 (38)
	**13a**	5·872	289 (25)

[a] The IR spectra were determined on a Perkin–Elmer model 12C single-beam spectrometer.
[b] In EtOH.

positive and the latter negative (Fig. 1, Table 4). It was possible to establish from the ORD measurements the equilibrium ratio of these two ketones. A solution of the ketones in dioxan was treated with 20% sulfuric acid (the final concentration of acid being ca 0·1M) and heated for 2 hr on a water bath. After the acid treatment, the epimeric ketones **3a** and **4a** gave almost identical ORD curves, indicating an equilibrium concentration of the two ketones (Fig. 1, Table 4). The ratio of the epimers at the equilibrium concentration, calculated from its molecular rotation value at the first extremum and from the corresponding values of the pure epimers was found to be ca. 4:1.†

In the androstane series, the ORD of the crystalline equilibrium mixture of **3b** and **4b** gave a Cotton effect of the same sign and of similar magnitude to the equilibrium mixture of the two ketones **3a** and **4a** in the cholestane series (Table 4).

The two epimeric A-nor-B-homo ketones **13a** and **14a** also gave Cotton effects of opposite sign, but the amplitude of the former ketone was much higher than that of the latter (Fig. 2, Table 4). The equilibrium ratio could be established using a similar procedure namely heating a solution of each of the epimeric ketones **13a** and **14a**

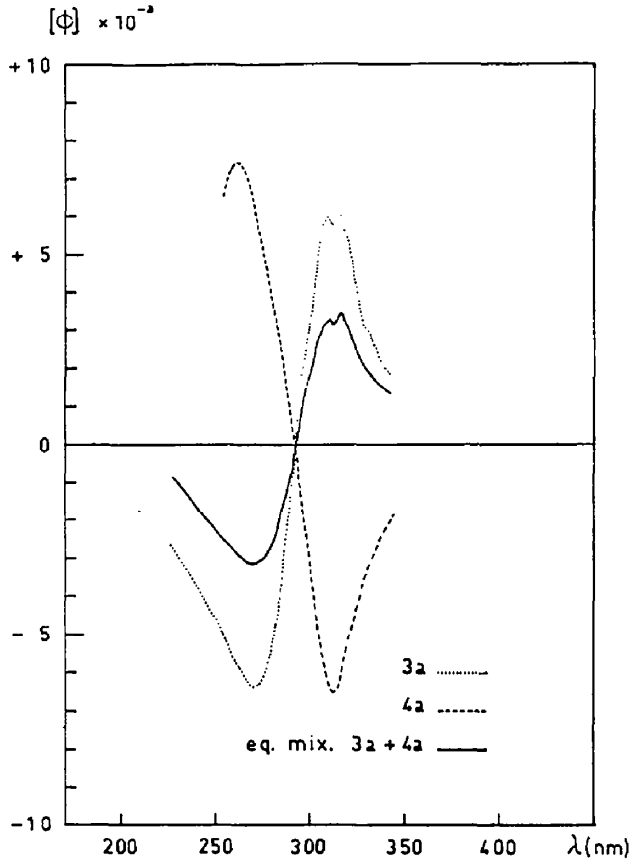


FIG. 1 ORD curves of the A-homo-B-nor-5-ketones **3a** and **4a** and of the equilibrium mixture of **3a** and **4a** in dioxan.

in dioxan in 0·1N H_2SO_4. The ratio of the two epimeric ketones was found to be 4:1,† the thermodynamically more stable epimer being the 4α-ketone **13a** (Fig. 2).

In the androstane series the two 4α and 4β ketones **13b** and **14b** gave similar Cotton effects to the respective compounds in the cholestane series (Table 4). The somewhat smaller value of the first extremum in **14b** could result from its partial epimerization. When treated with 0·1N acid, equilibration of each of the two ketones **13b** and **14b** was observed, as found from the ORD curve of the resulting solutions (Table 4). The positive amplitude of the Cotton effect showed the relatively higher stability of the 4α ketone **13b**; the ratio of **13b** to **14b** being also 4:1.

† The molar fraction of the epimeric ketones at equilibrium was calculated using the following relation:

$$N_A = \frac{[\phi]_0 - [\phi]_B}{[\phi]_A - [\phi]_B} \cdots$$

where N_A is the molar concentration of one of the epimers and $N_B = 1 - N_A$ the molar concentration of the other one. $[\phi]_A$ and $[\phi]_B$ being the molecular rotations at the first extremum of the two epimers respectively and $[\phi]_0$ the molecular rotation at the first extremum of the equilibrium mixture.

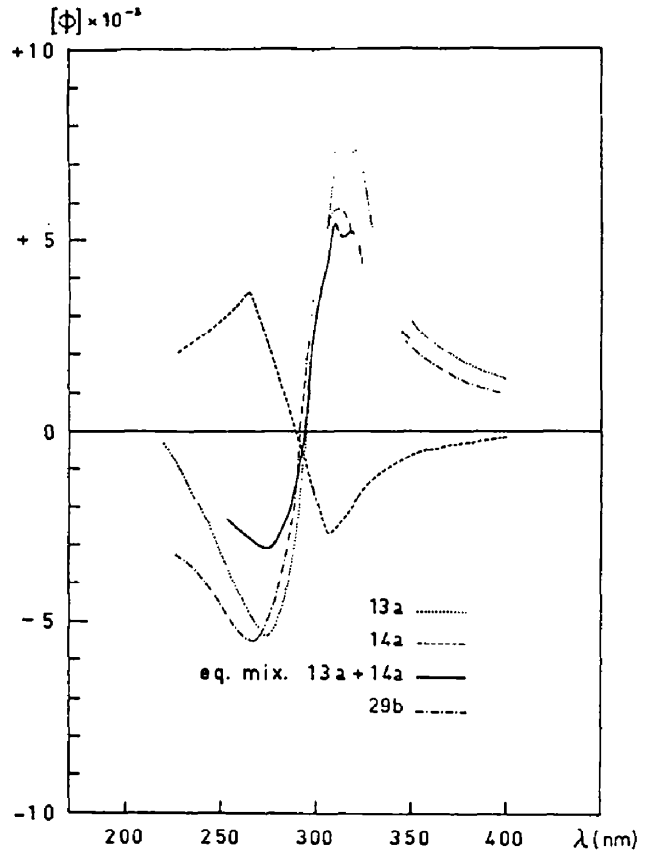


FIG. 2 ORD curves of the A-nor-B-homo-5-ketones **13a**, **14a** and **29b** and of the equilibrium mixture of **13a** and **14a** in dioxan.

The corresponding ketone in the estrane series, **29a**, showed a positive Cotton effect with amplitude similar to that observed in both 4α ketones **13a** and **13b** (Fig. 2, Table 4). This positive amplitude in **29a** is thus in accord with the assigned configuration of C-4. Acid treatment of **29a** did not change its Cotton curve to any observable extent, indicating that isomerisation to the 4β-ketone did not take place.

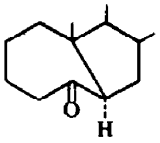
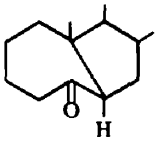
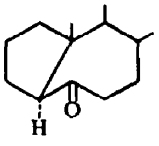
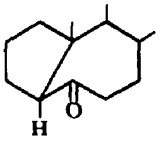
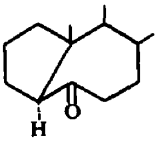
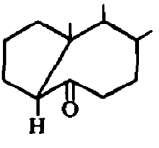
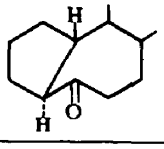
The zero rotational value for all the ketones measured, except the A-nor-B-homo-4β-ketone **14a** was at λ 292–293 mμ. The corresponding value of the latter was at 290 mμ. A similar hypsochromic shift was observed in the UV for the n → π* transition in this system.

NMR *measurements*

The spectra of the four types of ketones **3**, **4**, **13** and **14** were measured at room temperature in $CDCl_3$, CCl_4 and benzene and also in the former solvent at a temperature of −40° (Table 5).

In the four types of ketones, the chemical shifts of the C-18 Me protons in $CDCl_3$ and CCl_4 have similar values. On the other hand, the position of the C-19 Me

TABLE 4. ORD DATA FOR THE A-HOMO-B-NOR AND THE A-NOR-B-HOMOSTEROID 3, 4, 13 AND 14.

Compound		$[\phi] \times 10^{-2}$ [a]	$[\phi] \times 10^{-2}$ [a]	$[a]$ [b]	λ_0^c
	**4a**	−39°	+41°	−80°	293
	**3a**	+36	−38°	+74°	293
Equilibrium mixture of **3a** and **4a**		+20°	−17°	+37°	293
Equilibrium mixture of **3b** and **4b**		+11°	−16°	+27°	293
	**13a**	+78°	−58°	+136°	293
	**14a**	−27°	+36°	−63°	290
Equilibrium mixture of **13a** and **14a**		+55°	−33°	+88°	292
	**13b**	+60°			
	**14b**	−13°			
Equilibrium mixture of **13b** and **14b**		+45°			
	**29b**	+57°	−55°	+112°	292

[a] Molecular rotation.
[b] Amplitude.
[c] Wavelength at zero rotational value.

resonances vary considerably: in the ring A/B *cis*-ketones **3** and **14** they fall at comparably high fields and in the A/B-*trans* ketones **4** and **13** at low fields. These values indicate that in both A/B *cis* ketones **3** and **14** the C-19 Me is being shielded and in the A/B *trans* ketones **4** and **13** deshielded by the CO group.

More information on the relative positions of the C-19 Me groups and the CO function in the 7-membered rings was obtained from the values of the aromatic solvent induced shifts.[10] These shifts have been observed previously in normal keto-steroids and are described in the literature.[11] A comparison was made between those ketones possessing a similar 1:3 relation of the CO and C-19 Me groups and the ketone investigated here. Since the former compounds have a fixed and known conformation, this comparison may be an asset in conformational analysis of the 7-membered ketones.

In the 4-keto-5β-cholestane where the C-19 Me is equatorial in relation to the ring bearing the CO function the solvent induced shift is positive and comparatively large (0·24 ppm). In all other ketones the C-19 Me is axial to the ring A, and the shift is still positive but much smaller (0·06–0·15 ppm).[11] Since the A/B *cis* ketones **3** and **14** show similar solvent induced shift as the 4-keto-5β-cholestane—the relative position of the CO and the C-19 Me groups may be similar. In addition the C-19 Me protons of the former compound have the same chemical shift as in the ketones **3** and **14**.

Normal keto-steroids having an axial C-19 Me in relation to the ring bearing the CO group may be similarly compared with A/B *trans* ketone **4** and **13**. In all these compounds the aromatic solvent induced shifts are small, and the C-19 Me resonances fall at comparatively high fields. However it appears that in the ketones **4** and **13** there is still closer proximity of the CO and the C-19 groups than in the 6-membered ketones, since the solvent induced shifts in the former compounds are smaller than in the latter.†

A temperature effect was found to operate with the C-19 Me signal in the two A-homo-B-nor ketones **3** and **4**. In the ketone **3**, the C-19 Me resonance shifted to lower field with decrease of temperature and in the ketone **4** the shift was to higher field. These results indicate a possible conformational equilibria of the 7-membered rings in these two compounds.

The conformational analysis of the 7-membered steroids

Theoretical considerations show that the preferred conformation for a 7-membered ring system is the "twist chair" conformation.[13] In fused ring systems having 7-membered rings, more than one such conformation is generally possible and the distinction between the various possibilities is difficult. Recently a detailed Hendrickson's-method calculation was used for the assignment of conformation in some of the 7-membered ring-A steroids.[14]

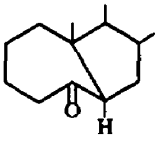
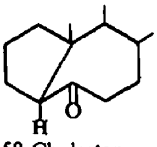
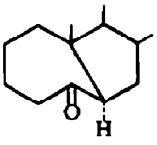
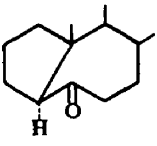
In order to establish the conformation of the four types of keto-steroids **3**, **4**, **13** and **14**, we have used the results of the NMR measurements which, as explained above, permit the establishment of the geometrical relationship between the C-19 Me and the CO function.

These results and the assignment of a "twist-chair" conformation to the 7-membered ring, led us to the following conformations for the ketones **3**, **4**, **13** and **14** (Fig. 3).

The "twist chair" conformations of 7-membered rings is designated by $TC_n(\pm)$;[14]

† C.f. for analogous shift in methylated cyclohexanones Fetison *et al.*[12]

TABLE 5. NMR DATA FOR THE A-HOMO-B-NOR AND THE A-NOR-B-HOMOSTEROIDS 3, 4, 13 AND 14 AND FOR 5β-CHOLESTAN-4-ONE AND 5α-CHOLESTANE-4-ONE

Compound		Protons at	$CDCl_3$ +30°	$CDCl_3$ −40°	CCl_4	C_6D_6	Δ_1[a]	Δ_2[b]	Δ_3[c]
	**3a**	C_{18}	0·67	0·67	0·65	0·64	+0·03	+0·01	0·00
		C_{19}	1·07[d]	1·11	1·05	0·86	+0·21	+0·25	−0·04
	**14a**	C_{18}	0·69	0·69	0·69	0·62	+0·07	+0·07	0·00
		C_{19}	1·07[d]	1·07	1·05	0·83	+0·24	+0·22	0·00
5β-Cholestan-4-one[e]		C_{18}	0·65			0·62	+0·03		
		C_{19}	1·12			0·88	+0·24		
	**4a**	C_{18}	0·67	0·67	0·65	0·59	+0·08	+0·06	0·00
		C_{19}	0·65[d]	0·63	0·65	0·64	+0·01	+0·01	+0·02
	**13a**	C_{18}	0·67	0·67	0·66	0·64	+0·03	+0·02	0·00
		C_{19}	0·67[d]	0·67	0·66	0·62	+0·05	+0·04	0·00
5α-Cholestan-4-one[f]		C_{18}	0·66		0·65	0·62	+0·04	+0·03	
		C_{19}	0·74		0·72	0·62	+0·12	+0·01	

[a] $\Delta_1 = CDCl_3 - C_6D_6$;
[b] $\Delta_2 = CCl_4 - C_6D_6$;
[c] $\Delta_3 = CDCl_3\ (+30°) - CDCl_3\ (-40°)$;
[d] The respective values for the C_{19} methyl of 17β-hydroxyandrostane derivatives **3b** and **4b** are: 1·08 and 0·64 ppm (in the equilibrium mixture) and for **14c** and **13c**: 1·08 and 0·70 ppm;
[e] E. Glotter and D. Lavie, *J. Chem. Soc.* (C) in press;
[f] Ref. 10.

where TC denotes twist-chair, n—the number of the C atom serving as the axis of the twist and the positive or negative sign designates the absolute direction of the twist. Thus, the respective conformations for **3**, **4**, **13** and **14** are $TC_3(-)$, $TC_3(-)$, $TC_6(-)$ and $TC_4(-)$.

The small temperature effect in the NMR (Table 6) shown by both A-homo-B-nor-ketones **3** and **4** may indicate an equilibrium of more than one conformation in these two ketones. Thus, in addition to the preferred $TC_3(-)$ conformations for the ketones **3** and **4**, other conformations like $TC_3(+)$, $TC_{10}(-)$ for **3** and $TC_4(+)$ for **4**, may be postulated to prevail in equilibrium. Lowering of the temperature may thus shift the equilibrium to some extent resulting in a higher proportion of the more stable

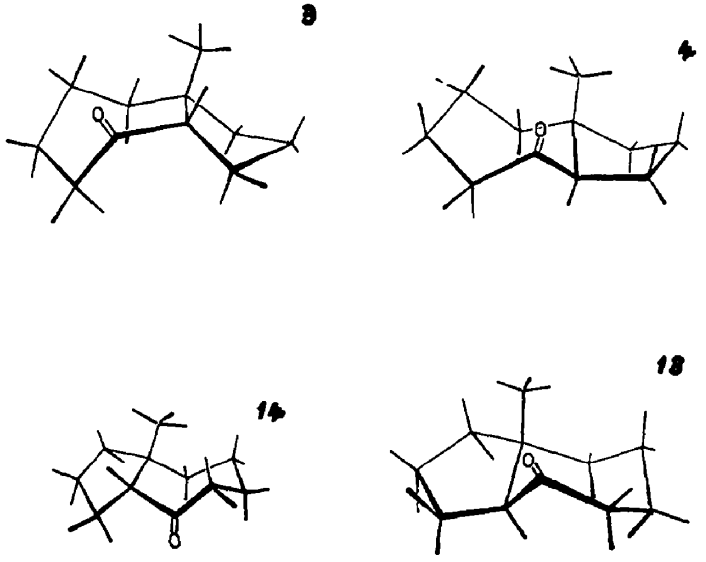


FIG. 3 Proposed conformation of the 7-membered rings in A-homo-B-nor-5-ketones 3 and 4 and in A-nor-B-homo-5-ketones 13 and 14.

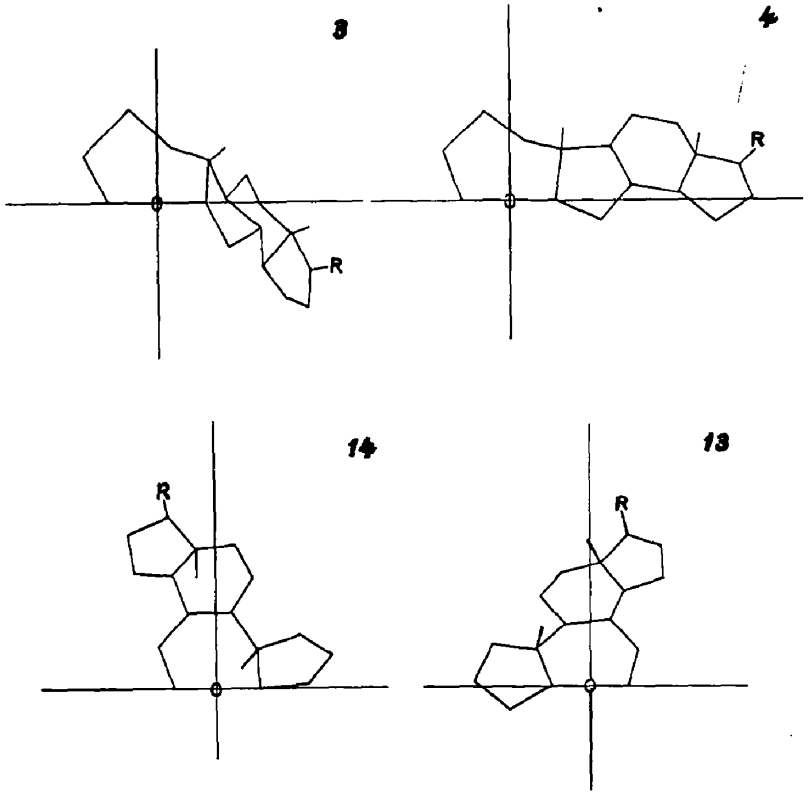
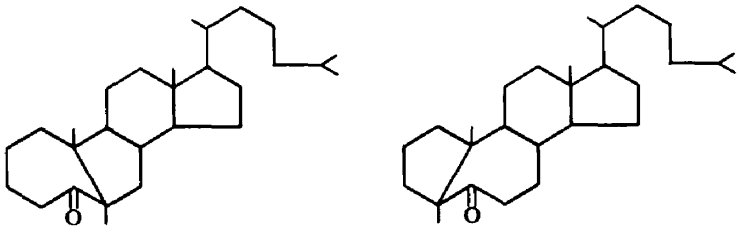


FIG. 4 "Octant rule" projections for the A-homo-B-nor-5-ketones 3 and 4 and for the A-nor-B-homo-5-ketones 13 and 14.

$TC_3(-)$ conformation as indicated by the direction of change of the chemical shift of the C-19 Me protons.

The ORD data are less suitable for determining the preferred conformations of the ketones **3**, **4**, **13** and **14**. The "octant rule" may be applied rigorously to 6-membered ring ketones, but less so for 7-membered ring ketones. In these it is not possible to fix the relative contributions to the Cotton effect amplitude of the atoms in various positions of the "octant" diagram. Nevertheless the "octant" diagrams for the four compounds were drawn (Fig. 4). It may be seen from these that a quantitative rough application of the "octant rule" leads to a sign prediction which agrees with the sign of the Cotton effect found experimentally.

The A-homo-B-nor and A-nor-B-homoketones **35** and **36** described by Kirk *et al.*,[15] exist presumably in similar conformation to the corresponding A/B *cis*-ketones **3** and **14**. This is indicated by the similarity of the chemical shifts of the C-19 protons in **35** and **36** (at 0·97 and 1·07 ppm)† to the shifts of A/B-*cis* ketones **3** and **14** (both at 1·07 ppm—Table 5). The additional Me group in **35** and **36** may however contribute to the Cotton effect of the CO chromophore. According to the "octant diagrams" (Fig. 4) this contribution is negative in **35** and positive in **36**, which accords with the observed weak positive effects in both compounds.[15]



35 **36**

CHART VI

EXPERIMENTAL

All m.ps were taken in capillaries and were uncorrected, the IR spectra were determined on a Perkin–Elmer Infracord, and the rotations were done in $CHCl_3$ soln. UV absorption spectra were measured on a Cary 14 spectrophotometer. The NMR spectra were determined on a Varian A-60 spectrometer, peak positions are indicated in ppm down-field from TMS serving as internal reference. The ORD spectra were determined on a Jasco ORD/UV-5 instrument using cells of 1-mm width. Mass spectra were measured with an Atlas CH-4 instrument, samples being introduced directly into the ion source.

5α-Tosyloxy-cholestan-5α-ol (**2b**)

A soln of 800 mg **2a**[3] (m.p. 177–179°, $[\alpha]_D$ +16°) and 1·0 g *p*-tosyl chloride in 40 cc dry pyridine was left overnight at room temp. The soln was poured into a mixture of ice water and $NaHCO_3$ aq and extracted with ether. Crystallization from EtOH afforded 920 mg of **2b** m.p. 122–123°; $[\alpha]_D$ +18°. (Found: C, 73·73; H, 9·81; S, 5·15. Calc. for $C_{34}H_{54}O_4S$: C, 73·08; H, 9·74; S, 5·73%).

A-Homo-B-nor-6β-cholestan-5-one (**3a**) *and A-homo-B-nor-6α-cholestan-5-one* (**4a**).

(a) A soln of 560 mg **2b** in 20 cc of dry t-BuOH containing t-BuOK (from 40 mg K) was left at 25° for

† We are indebted to Dr. D. N. Kirk, Westfield College, London, for this information.

15 mins. Extraction with ether and crystallization of the residue (370 mg) from MeOH afforded 315 mg of **3a**; m.p. 125–126°; $[\alpha]_D$ +19°. (Found: C, 83·97; H, 11·87. Calc. for $C_{27}H_{46}O$: C, 83·87; H, 11·99%).

(b) A soln of 150 mg **2b** in 20 cc DMF and 200 mg $CaCO_3$ were heated for 8 hr on a steam bath. Filtration, extraction of the filtrate with ether and crystallization from MeOH gave 85 mg of **3a** m.p. 123–125°; $[\alpha]_D$ +21°.

(c) A soln of 150 mg of **2** in 2 cc benzene was passed through a column of 15 g alumina (Merck acid washed). Elution after 6 hr with pentane–benzene 9:1 gave 20 mg of **3a**, m.p. 125–126° (after crystallization from ether–MeOH); $[\alpha]_D$ +19°, identical with the product obtained in (a) and (b). Elution with the same solvents gave 60 mg of a mixture m.p. 106–109°. Further elution with benzene–ether 9:1 and 4:1 gave 20 mg of **4a** m.p. 136–137° (after crystallisation from ether–MeOH) $[\alpha]_D$ −10°. (Found: C, 83·85; H, 11·84. Calc. for $C_{27}H_{46}O$: C, 83·87; H, 11·99%). The material of m.p. 106–109° consisted according to the IR of a mixture of **3a** and **4a** (4:1).

Equilibration of **3a** *and* **4a**

(a) A soln of 500 mg **3a** in 25 cc dioxan containing 0·4 cc 20% H_2SO_4 was heated on a water bath for 2 hr in atmosphere of N_2. The crystalline product isolated from ether, m.p. 106–110° was chromatographed on acid washed alumina. The first fraction eluted with pentane–ether 9:1 gave 120 mg of **3a**, m.p. 124–125°. The second one eluted with the same solvent gave a mixture of **3a** and **4a**, m.p. 103–110° (in a ratio of ca 4:1). The third fraction eluted with the same solvents gave 25 mg of **4a** m.p. 132–134.

(b) A soln of 50 mg of **4a** in dioxan containing H_2SO_4 was heated as above. Isolation and chromatography on alumina led to a similar mixture of **3a** and **4a** as above.

17β-*Benzyloxy-androst-5-en* (**1b**)

A soln of 2·2 g 17β-hydroxy-androst-5-ene (m.p. 162–164°) and 5 cc benzoyl chloride in 20 cc dry pyridine was refluxed for 1 hr. The excess of reagent was destroyed with hot water and the mixture estracted with ether. Crystallization from ether–MeOH afforded 1·85 g of **1b** m.p. 148–150° $[\alpha]_D$ −13°. (Found: C, 82·37; H, 8·90. Calc. for $C_{26}H_{34}O_2$: C, 82·49; H, 9·05%).

17β-*Benzyloxy-androstane-5α,6α-diol* (**2c**)

A soln of 1·6 g **1b** and 1·2 g OSO_4 in 40 cc pyridine was left for 3 days at room temp, then treated with a soln of 5 g $NaHSO_3$ and shaken for ½ hr. The product was isolated from EtOAc, crystallized from acetone–hexane to give 1·5 g of **2c**, m.p. 234–235°; $[\alpha]_D$ +43·5°. (Found: C, 75·56; H, 8·74. Calc. for $C_{26}H_{36}O_4$: C, 75·69; H, 8·80%).

17β-*Benzyloxy-6α-tosyloxy-androstan-5α-ol* (**2d**)

A soln of 1·2 g of **2c** and 2·5 g *p*-tosyl chloride was kept 2 days at room temp. Isolation from EtOAc and crystallization of the product from ether–MeOH gave 1·8 g, of **2d** m.p. 129–130°; $[\alpha]_D$ +34°. (Found: C, 69·97; H, 7·44; S, 5·32. Calc. for $C_{33}H_{42}O_6S$: C, 69·94; H, 7·47; S, 5·65%).

17β-*Benzyloxy-A-homo-B-nor-6β-androstan-5-one* **2d** (**3c**)

To a soln of 1·0 g of **2d** in 80 cc DMF was added 200 mg $CaCO_3$ and the mixture was heated for 8 hr on a steam bath in a N_2 atm. Filtration of the carbonate, extraction with ether and crystallization from ether–MeOH afforded 0·62 g of **3c** m.p. 120–122°; $[\alpha]_D$ +51°; λ_{max}^{KBr} 5·85, 5·91 μ. (Found: C, 79·26; H, 8·69. Calc. for $C_{26}H_{34}O_3$: C, 79·15; H, 8·69%).

17β-*Hydroxy-A-homo-B-nor-6β-androstane-5-one* **3b** *and* 17β-*hydroxy-A-homo-B-nor-6α-androstane-5-one* **4b**

(a) A soln of 280 mg of **2d** in 20 cc of dry t-BuOH containing t-BuOK (prepared from 50 mg K) was refluxed for ½ hr, in a N_2 atm. Water (2 cc) was added and the boiling was continued for another ½ hr. Extraction with EtOAc and chromatography on 5 g silica gel afforded 135 mg of a mixture of **3b** and **4b** which after crystallization from ether showed m.p. 153–155°; $[\alpha]_D$ +5°; λ_{max}^{KBr} = 5·91 μ. (Found: C, 78·57; H, 10·32. Calc. for $C_{19}H_{30}O_2$: C, 78·57; H, 10·41%).

(b) Hydrolysis of **3c** with t-BuOK in t-BuOH gave in a quantitative yield the mixture of **3b** and **4b** m.p. 153–155°.

Reduction of **3a** *to the hydrocarbon* **5**

A soln of 50 mg of **3a**, 1·5 cc hydrazine hydrate and 10 cc diethylene glycol was boiled under reflux for 2 hr and then a soln of KOH (1·0 g) in water (1 cc) was added, the reaction mixture heated to 195°, this temp being maintained for 2 hr. The product was isolated from ether and crystallized from MeOH to give 28 mg of **5**, m.p. 71–72°, $[\alpha]_D$ +29·5°. (Found: C, 86·87; H, 13·03. Calc for $C_{27}H_{48}$: C, 87·02; H, 12·98%).

A-*Homo*-B-*nor*-5β-*cholestan*-4-*one* (**6**)

A soln of 200 mg of **7**[4] (m.p. 64–65°; $[\alpha]_D$ +16°) in 40 cc of 1:1 mixture of ether–MeOH was treated with excess of an ethereal soln of diazomethane. After standing overnight at room temp, the excess of diazomethane was destroyed with a few drops of AcOH and the solvent evaporated to dryness *in vacuo*. Chromatography on 6 g of alumina afforded 120 mg of crystals (eluted with pentane–benzene 9:1). Crystallization from MeOH gave 95 mg of **6** m.p. 78–80° $[\alpha]_D$ +21°. (Found: C, 84·07; H, 11·89. Calc for $C_{27}H_{46}O$: C, 83·87; H, 11·99%).

A-*Homo*-B-*nor*-6β-*cholestane* (**5**)

The ketone **6**, 50 mg, was reduced with a soln of hydrazine and NaOH in diethylene glycol as described. Crystallization from MeOH gave 32 mg of hydrocarbon m.p. 70–72°; $[\alpha]_D$ +29; identical with **5**, obtained previously from the Wolff–Kishner reduction of **3a**.

A-*Homo*-B-*nor*-6β-*cholestan*-5β-*ol* (**8a**)

A soln of 300 mg **3a** in 25 cc dry ether was added to a suspension of 75 mg LAH in 25 cc dry ether. After ½ hr of reflux, the product was isolated from ether and crystallized from ether–MeOH to give 240 mg of **8a**, m.p. 57–59°; $[\alpha]_D$ +46°.

A-*Homo*-B-*nor*-*cholest*-5-*ene* (**9**)

(a) A soln of 50 mg **8a** and 125 mg of *p*-tosyl chloride in 10 cc dry pyridine was left at room temp for 3 days. The soln was poured in ice water and $NaHCO_3$ aq and extracted with ether. Crystallization from ether–MeOH afforded 60 mg of **8b** m.p. 97–98°, $[\alpha]_D$ +21°. (Found: C, 75·69; H, 10·08; S, 5·13. Calc for $C_{34}H_{54}O_3S$: C, 75·23; H, 10·03; S, 5·89%).

A soln of 40 mg **8b** in 15 cc ether was added to a soln of 20 mg LAH in 15 cc ether. After being heated under reflux for 24 hr, the product was isolated from ether to give 22 mg of **9**, m.p. 84–86°; $[\alpha]_D$ −2°; λ_{max}^{KBr} 12·2 μ; λ_{max}^{EtOH} 211 mμ (ε 6800). The compound gave a positive test with tetranitromethane. (Found: C, 87·79; H, 12·31. Calc. for $C_{27}H_{46}$: C, 87·49; H, 12·51%).

(b) A soln of 40 mg of **8a** and 0·15 cc freshly distilled mesyl chloride in 10 cc dry pyridine was kept overnight at room temp. The crude mesylate, **7c**, 65 mg, isolated from ether was obtained as an oil, and was used as such for the next reaction.

A solution of **8a**, 100 mg, in 20 cc 2-butanone was treated with 300 mg KI and refluxed for 20 hr. The product isolated from ether, was chromatographed on 5 g alumina. Elution with pentane and ether gave 55 mg of the olefin **9** m.p. 83–84° identical with the sample described under (a).

A soln of 25 mg of **9** in 10 cc EtOAc was reduced with H_2, in the presence of 15 mg 5% Pd-C for 3 hr. Filtration of the catalyst, evaporation of the solvent and crystallization of the residue from ether–MeOH afforded 15 mg of **5**, m.p. 69–71°; $[\alpha]_D$ +31°; identical with the hydrocarbon obtained by Wolff–Kishner reduction of **3a**.

A-*Nor*-B-*homo*-*cholestan*-5-*one* (**13a**)

A soln of 560 mg of **11a**[5] in 30 cc DMF was treated with 100 mg $CaCO_3$ and was refluxed for 24 hr, under N_2. Filtration of the carbonate, extraction of the filtrate with ether and crystallization from MeOH gave 360 mg of **13a**, m.p. 86–88°; $[\alpha]_D$ +125°. (Found: C, 84·06; H, 12·05. Calc for $C_{27}H_{46}O$: C, 83·87; H, 11·99%).

A-*Nor*-B-*homo*-4β-*cholestan*-5-*one* (**14a**)

A soln of 100 mg of **12a**[5] in 10 cc DMF and 100 mg $CaCO_3$ were refluxed for 24 hr under N_2. Filtration of the carbonate, extraction of the filtrate with ether, and crystallization from MeOH gave 70 mg of **14a** m.p. 94–95° $[\alpha]_D$ −27°. (Found: C, 84·07; H, 11·88. Calc for $C_{27}H_{46}O$: C, 83·87; H, 11·99%).

Equilibration of ketones **13a** and **14a**

(a) The ketone **13a**, 300 mg, was dissolved in 25 cc of a soln of dioxan containing 0·4 cc H_2SO_4 (20%) and heated at 100°, under N_2 for 2 hr. The product was extracted from ether and chromatographed on 10 g alumina. Elution with pentane benzene 9:1 and crystallization from MeOH afforded 32 mg of **14a**, m.p. 94–95°. Elution with pentane benzene 9:1 and 4:1 and crystallization from ether–MeOH gave 230 mg of **13a** m.p. 86–88°.

(b) A soln of 560 mg of **13a** in 20 cc t-BuOH containing t-BuOK (prepared from 35 mg K) was refluxed under N_2 for 1 hr. The crude product was chromatographed on 15 g alumina. Elution with pentane–benzene 9:1 and crystallization from ether–MeOH gave 55 mg of the ketone **14a** m.p. 94–95°. Elution with pentane–benzene 9:1 and 4:1 and crystallization from ether–MeOH gave 400 mg of **13a** m.p. 86–88°.

(c) The ketone **14a** (10 mg) was heated in dioxan containing H_2SO_4 and the product chromatographed on alumina, as described above, yielding 15 mg of **14a** and 75 mg of **13a**.

(d) The ketone **14a** (200 mg) was heated in t-BuOH containing t-BuOK and the product chromatographed on alumina as described above, to yield 25 mg of **14a** and 100 mg of **13a**.

17β-*Benzyloxy-androsten-4-ene* (**10b**)

Compound **10a** (3.8 g; m.p. 151–153°, $[\alpha]_D$ +51°)[16] was benzoylated with benzoyl chloride in pyridine. Crystallization from MeOH afforded 3·3 g of **10b** m.p. 138–139°, $[\alpha]_D$ +122°. (Found: C, 82·25; H, 8·99. Calc for $C_{26}H_{34}O_2$: C, 82·49; H, 9·05%).

17β-*Benzyloxy-4α,5α-diol* (**12c**)

A soln of 2·4 g diol **10b** and of 1·8 g OsO_4 in 50 cc pyridine was left for 2 days at room temp. A soln of 3 g of $NaHSO_3$ in 50 cc water was added and the mixture shaken for ½ hr. The product was isolated from EtOAc and crystallized from MeOH to give 2·2 g of **12d** m.p. 230–232°, $[\alpha]_D$ +32·5°. (Found: C, 75·34; H, 8·60. Calc for $C_{26}H_{36}O_4$: C, 75·69; H, 8·80%).

17β-*Benzyloxy-4α-tosyloxy-androstan-5α-ol* (**12d**)

The diol **12c** was tosylated with 2 g tosyl chloride in pyridine. Crystallization from acetone gave 1·7 g of **12d** m.p. 166–167° (dec) $[\alpha]_D$ +53°. (Found: C, 69·98; H, 7·45, H, 5·43. Calc for $C_{33}H_{42}O_6S$: C, 69·94; H, 7·47; S, 5·65%).

17β-*Benzyloxy*-A-*nor*-B-*homo-androstan-5-one* (**14b**)

A soln of 570 mg **12d** in 30 cc DMF containing 100 mg $CaCO_3$ was refluxed for 24 hr under N_2. Filtration of the carbonate, extraction of the filtrate with ether and crystallization from acetone–hexane afforded 370 mg of **14b** m.p. 166–168°, $[\alpha]_D$ +33° λ_{max} 5·85, 5·91 μ. (Found: C, 79·22; H, 8·59. Calc for $C_{26}H_{34}O_3$; C, 79·15; H, 8·69%).

17β-*Hydroxy*-A-*nor*-B-*homo-androstane-5-one* (**13c** *and* **14c**)

A soln of 750 mg of **12d** in 60 cc of t-BuOH containing t-BuOK (prepared from 150 mg K) was refluxed for 1 hr, under N_2. MeOH, 2 cc, was added and the reflux continued for another ½ hr. The product was isolated from ether and chromatographed on 12 g silica gel. Elution with benzene gave 48 mg of material which was crystallized from acetone–hexane to give 40 mg of **14c** m.p. 162–163°, $[\alpha]_D$ +155°. (Found: C, 78·35; H, 10·50. Calc for $C_{19}H_{30}O_2$: C, 78·57; H, 10·41%).

Elution with benzene–ether 9:1 and 4:1 and crystallization from ether–MeOH gave 270 mg of **13c** m.p. 126–128°; $[\alpha]_D$ +20°.

Equilibration of the keto–alcohols **13c** *and* **14c**

(a) A soln of 200 mg of **13c** in 20 cc dioxan containing 0·2 cc 20% H_2SO_4 was heated at 100° for 2 hr. The product was extracted with ether and chromatographed on 6 g silica. Elution with benzene gave 25 mg of **13c** m.p. 160–162° (after crystallization from MeOH). Elution with benzene–ether 9:1 and crystallization from MeOH gave 155 mg of **14a** m.p. 125–128° $[\alpha]_D$ +22°.

(b) A soln of 50 mg of **14c** was treated as above. Chromatography and crystallization yielded 5 mg of **13c** and 35 mg of **14c**.

Benzoylation of the keto-alcohols **13c** *and* **14c**

The keto-alcohol **13c** (20 mg) was benzoylated with benzoyl chloride in pyridine. The isolated benzoate, **13b**, 25 mg, had m.p. 179–180°, $[\alpha]_D$ +143° (after crystallization from acetone–hexane).

The keto-alcohol **14c**, 100 mg was benzoylated as above. Crystallization of the product from acetone–hexane afforded 90 mg of **14b** m.p. 166–168° $[\alpha]_D$ +33°.

3β-*Acetoxy*-B-*homo-cholestan-one* (**18**)

A soln of 5 g of **16**[17] in 60 cc acetone cyanohydrin and 1·0 cc 10% NaOH aq was shaken for 2 hr at room temp. The soln was poured into 2 l. ice-water containing 5 cc AcOH and the solid was filtered off. A suspension of the solid in 100 cc glacial AcOH was hydrogenated with 1·5 g pre-reduced Adams catalyst until 1·9 mole equivs of H_2 were absorbed. The mixture was diluted with 2 l. water, filtered through Celite and the clear soln of **17**, cooled to −10° and treated dropwise with stirring with a cold soln of 15 g $NaNO_2$ in 75 cc water (the temp of the reaction mixture did not rise above 0°). The soln was left overnight at room temp, then the ppt was filtered off and washed with water to give 4·3 g of an amorphous product, λ_{max}^{KBr} 5·78, 5·88 μ, which contained the product **18**.

A mixture of this solid, 175 cc EtOH, 20 cc AcOH and 8 g Girard T reagent was refluxed for 2 hr. Ethylene glycol, 175 cc, was then added and the alcohol evaporated under reduced press. After cooling, the mixture was extracted with ether and the ether extracts washed with ethylene glycol. The glycol fractions were diluted with 50 cc water, then 0·3 cc conc HCl was added and the mixture heated on a steam bath for 15 min. Extraction with ether afforded 900 mg of **18**, which after crystallization from a small volume of MeOH had a m.p. 105–107°; $[\alpha]_D$ −53°; λ_{max}^{KBr} 5·78 and 5·88 mμ. (Found: C, 78·50; H, 11·20. Calc for $C_{30}H_{50}O_3$: C, 78·55; H, 10·99%).

B-*Homo-cholestane*-3-*one* **19b**

The keto-acetate **18**, 540 mg, was reduced by the Wolff–Kishner procedure as described. The crude product, **19a** (340 mg) which could not be brought to crystallization was oxidized with pyridinium chromate (prepared from 250 mg CrO_3 and 3 cc pyridine) at room temp for 2 days. The pyridine was evaporated under vacuum and the residue washed with several portions hot benzene. Evaporation of the solvent and chromatography of the product on 10 g alumina afforded 295 mg of **19b** (eluted with pentane–benzene 4:1), which after crystallization from MeOH showed a m.p. 81–82°; $[\alpha]_D$ +52°. (Found: C, 83·94; H, 12·04. Calc for $C_{28}H_{48}O$: C, 83·93; H, 12·08%).

A-*Nor*-B-*homo-cholestane*-2-*one* **23**

A mixture of 250 mg of **19b** in 10 cc anhyd thiophene-free benzene 0·5 cc HCOOEt and 150 mg NaH was stirred for 3 days under N_2. MeOH (2 cc) was added and the soln diluted with water. The basic soln was extracted with ether and the aqueous layer was then acidified with ice cold, dil HCl and extracted with ether. The ether layer yielded, 220 mg of an oily hydroxymethylene derivative **20**. A soln of this material in 15 cc CH_2Cl_2 was cooled to −20°, and O_3 was passed through, until a blue colour persisted. Then 4 cc H_2O_2 (30%) was added and the soln left at room temp overnight. It was extracted with ether, and the crude product, **21a**, (140 mg) was esterified with an excess of diazomethane in ether. Chromatography of the product on alumina and elution with pentane–benzene 1:1 afforded 100 mg of **21b**. This material was dissolved in 20 cc dry benzene and refluxed with t-BuOK (prepared from 25 mg K) for 16 hr. The reaction mixture was cooled and acidified with dil HCl. Extraction with ether afforded 85 mg of **22** λ_{max}^{KBr} 5·75 and 5·84 mμ. A soln of **22**, and 2 cc conc HCl in 6 cc AcOH was refluxed for 1 hr, then was diluted with water and extracted with ether. Chromatography of the residue over alumina, elution with pentane–benzene 4:1 and crystallization from MeOH gave **23**, 35 mg, m.p. 64–65°, $[\alpha]_D$ +115°; λ_{max}^{KBr} 5·75 μ. (Found: C, 83·90; H, 11·78. Calc. for $C_{27}H_{46}O$: C, 83·87; H, 11·78%).

A-*Nor*-B-*homo*-5α-*cholestane* (**15**)

(a) A soln of **23**, (20 mg) and 1·5 cc hydrazine hydrate in 10 cc diethylene glycol was heated under reflux for 2 hr. KOH, 1·0 g in 1 cc water was added and the soln slowly distilled until its internal temp reached 195° and then kept at this temp for 2 hr. The material was isolated from ether and was chromatographed on alumina. The hydrocarbon **15**, eluted with pentane, as an oil had $[\alpha]_D$ +21°; λ 200 mμ (ε, 450). (Found: C, 87·30; H, 12·75. Calc for $C_{27}H_{48}$: C, 87·02; H, 12·98%).

(b) A soln of 50 mg **13a** was reduced in an analogous way as described under (a). Chromatography on 3 g alumina and elution with pentane afforded 31 mg of **15** $[\alpha]_D$ +21° identical with the compound described under (a).

Lithium aluminium hydride reduction of **13a** *and* **14a**

(a) A soln of 200 mg of **13a** was treated dropwise with a soln of 50 mg LAH in 5 cc ether. After being left at room temp for 2 hr the product was isolated from ether. Chromatography on alumina and elution from ether gave 160 mg of oily **25a**.

(b) A soln of 100 mg of **14a** was reduced with LAH (30 mg) in ether. The product isolated from ether was crystallized from a small volume MeOH to give 90 mg of **26a**. M.p. 93–94° $[\alpha]_D$ +12.

A-*Nor*-B-*homo-cholest-4-ene* **24**

(a) A soln of 100 mg of **25a** in 5 cc dry pyridine was treated with 0·5 cc methanesulfonyl chloride and left overnight at room temp. The crude **25b** (115 mg) isolated from ether was dissolved in 20 cc THF, treated with a soln of 50 mg LAH in 5 cc THF and refluxed for 2 days. Isolation from ether, followed by chromatography and elution with pentane gave, 60 mg of oily **24**: λ_{max}^{KBr} 12·43 μ λ_{max}^{EtOH} 207 mμ (ε, 4800).

(b) A soln of 100 mg of **26a** in pyridine was treated with methanesulfonyl chloride and then the product **26b** with LAH as described under (a). Chromatography on alumina gave 50 mg of **24** identical with the product described under (a).

Catalytic reduction of the olefin **24**

A soln of 75 mg **24** in 5 cc EtOH were shaken with H_2 in the presence of 25 mg Pd–C (10%) for 3 hr. Filtration, chromatography of the filtrate on 3 g alumina, and elution with pentane gave 60 mg of **15** $[\alpha]_D$ +26° identical with the product obtained from **16**, as described.

Hydroxylation of 17β-*acetoxyestr-4-en* **27** *with osmium tetroxide*

A soln of 2·5 g of **27**[7] and of 2·2 g OsO_4 in 80 cc pyridine was allowed to stand for 3 days at room temp, and then was shaken with a soln of 5·0 g $NaHSO_3$ in 80 cc water for 30 min. The product was isolated from EtOAc and chromatographed on 80 g alumina. Elution with pentane–ether 1:4 afforded 1·98 g of **28a** m.p. 201–203° (after crystallization from acetone) $[\alpha]_D$ +14°. (Found: C, 71·36; H, 9·52. Calc for $C_{20}H_{32}O_4$: C, 71·39; H, 9·59%). The corresponding diacetate had m.p. 143–145° (after crystallization from ether) $[\alpha]_D$ +13°.

17β-*Acetoxy-4-tosyloxy-estran-5-ol* **28b**

A soln of, 1·2 g, **28a** and 2·0 g *p*-tosyl chloride in 5 cc pyridine was left for two days at room temp. The product was isolated from EtOAc and chromatographed on 50 g alumina. Elution from benzene–ether 9:1 gave 1·5 g of **28b** m.p. 146–147° $[\alpha]_D$ −19° (after crystallization from acetone–hexane). (Found: C, 65·84; H, 7·90; S, 6·46. Calc for $C_{27}H_{38}O_6S$: C, 66·10; H, 7·81; S, 6·52%).

17β-*Acetoxy*-A-*nor*-B-*homo*-4β-*estran-5-one* **29a**

(a) A soln of 1·25 g of **28b** in 50 cc DMF and 200 mg $CaCO_3$ was refluxed for 16 hr under N_2. Filtration, extraction of the filtrate with ether, chromatography on 25 g alumina and elution with pentane–ether 9:1 gave 520 mg of **29a** (after crystallization from pentane) m.p. 98–100° $[\alpha]_D$ +71°; λ_{max}^{KBr} 5·75; 5·91 μ λ_{max}^{MeOH} 284 mμ (ε 52). (Found: C, 75·33; H, 9·42. Calc for $C_{20}H_{30}O_3$: C, 75·43; H, 9·50%). Hydrolysis of 200 mg **29a** was effected by refluxing for 1 hr with KOH in MeOH. Crystallization from acetone:hexane gave 155 mg of **29b** m.p. 125–126° $[\alpha]_D$ +100°. (Found: C, 77·97; H, 10·28. Calc for $C_{18}H_{28}O_2$: C, 78·21; H, 10·21%), identical with an authentic sample.

When 200 mg of **29a** in 10 cc dioxan containing 0·1 cc 20% H_2SO_4 was heated at 100° for 2 hr, 150 mg of **29b** m.p. 124–126° resulted. Reacetylation of **29b** with pyridine and Ac_2O regenerated **29a** in almost quantitative yield.

3β,17β-*Diacetoxy*-4α,5α-*dihydroxy-androstane* (**31a**)

A soln of 2·5 g of **30a**[18] m.p. 102–104°, $[\alpha]_D$ +73° and 2·0 g OsO_4 in 60 cc pyridine was left for 3 days at room temp and then was shaken with a soln of 3·6 g $NaHSO_3$ in 50 cc water for 30 min. The material was isolated from EtOAc and crystallized from MeOH to give 1·95 g of **31a** m.p. 213–215° $[\alpha]_D$ +5°. (Found: C, 67·53; H, 9·00. Calc for $C_{23}H_{36}O_6$: C, 67·62; H, 8·88%).

3β,17β-*Diacetoxy-4α-tosyloxy-androstan-5α-ol* (**31b**)

A soln of 1·5 g **31a** and 2·0 g *p*-tosylchloride in 80 cc dry pyridine was refluxed for 8 hr. The product was isolated from EtOAc and crystallized from ether to give 1·2 g of **31b** m.p. 220–222°. (Found: C, 63·64; H, 8·06. Calc for $C_{30}H_{42}O_8S$: C, 64·04; H, 7·52%).

17β-*Hydroxy-3-aldehydo-A-nor-androst-3-ene* (**32a**)

A soln of 1·0 g **31b** in 100 cc methanolic 4% KOH was left overnight at room temp. The product was isolated from ether, and crystallized from ether–pentane to give 515 mg of **32a** (17β-OH) m.p. 159–161°; λ_{max}^{KBr} 6·02 μ λ_{max}^{EtOH} 256 (ε, 13,800) $[\alpha]_D$ +96°. Acetylation of **32a** with Ac_2O in pyridine and crystallization from MeOH gave **32a** (17β-OAc) m.p. 116–118° $[\alpha]_D$ +70°; λ_{max}^{KBr} 5·76, 6·02 μ; λ_{max}^{EtOH} 256 mμ (ε, 14,000). (Found: C, 75·94; H, 8·80. Calc for $C_{21}H_{30}O_3$: C, 76·32; H, 9·15%).

The dinitrophenylhydrazone of **32a** (17β-OAc) had m.p. 234–236°; λ_{max}^{EtOH} 223, 260, 296, 391 mμ. (Found: C, 62·83; H, 6·64; N, 10·77. Calc for $C_{27}H_{34}O_6N_4$: C, 63·51; H, 6·71; N, 10·97%).

Hydrolysis of **32** (17β OAc) with H_2SO_4 aq in MeOH reconverted it to **32a** (17β-OH) m.p. 155–161°, $[\alpha]_D$ +96°.

Catalytic reduction of the aldehyde **32a**

A soln of 200 mg of **32a** in 20 cc EtOAc was hydrogenated in the presence of 25 mg Pd–C. Filtration of the catalyst and evaporation of the solvent gave 190 mg of **33**. Its semicarbazone was crystallized from MeOH and had m.p. 208–210°; λ_{max}^{MeOH} 228 mμ (ε 7·800), and on heating with AcOH and pyruvic acid regenerated **32a**.

Synthesis of 3-aldehydo-17β-acetoxy-A-nor-androst-3-ene (**32a**)

A soln of 700 mg of **10**, (17β-OAc) in 150 cc MeOH and 15 cc CH_2Cl_2 was cooled to −65°. A stream of O_2 containing 3% O_3 was passed through this soln until a faint blue coloration persisted and then treated with 3 drops dimethyl phosphite. The soln was allowed to come to room temp the solvent evaporated *in vacuo*, and residue heated at 100° at 1 mm (λ_{max} 3·70 μ and 5·85 μ).

The resulting crude **34**, was dissolved in 10 cc MeOH containing 100 mg NaOMe, and left for 14 hr at room temp. The product was isolated from ether, acetylated with Ac_2O and pyridine, and chromatographed on 15 g alumina. Elution with pentane–benzene 1:1 gave 330 mg of **32a** m.p. 113–116° identical with the product described above.

3β,17β-*Diacetoxy-4α,5α-dihydroxy-estrane* (**31c**)

Hydroxylation of 1·5 g **30b**[19] (m.p. 138–139° $[\alpha]_D$ −23°) with 1·2 g OsO_4 as described gave 1·1 g of **31c** m.p. 194–196° $[\alpha]_D$ +16° (after crystallization from MeOH). (Found: C, 67·10; H, 8·76. Calc for $C_{22}H_{34}O_6$: C, 66·98; H, 8·69%).

3β,17β-*Diacetoxy-4α-tosyloxy-estran-5α-ol* (**31d**)

Tosylation of 1·0 g of **31c** as described and crystallization from acetone afforded 1·0 g of **31d** m.p. 212–214°, $[\alpha]_D$ +41°. (Found: C, 63·22; H, 7·25; S, 5·55. Calc for $C_{29}H_{40}O_8S$: C, 63·49; H, 7·35; S, 5·83%).

17β-*Acetoxy-A-nor-estr-3-en* (**32b**)

A soln of 0·5 g of **31d** in 50 cc methanolic 4% KOH was refluxed for 1 hr under N_2. The product was isolated from ether and then acetylated with Ac_2O and pyridine. The acetate was crystallized from MeOH to give 135 mg of **32b** m.p. 147–148° $[\alpha]_D$ +40°, λ_{max}^{KBr} 3·60, 5·75, 6·05 and 6·13 μ; λ_{max}^{MeOH} 256 mμ (ε, 16,000). (Found: C, 76·03; H, 8·96. Calc for $C_{20}H_{28}O_3$: C, 75·91; H, 8·92%). Hydrolysis of **32b** with H_2SO_4 aq in MeOH gave oily **32b** (17β-OH) λ_{max}^{KBr} 3·60, 6·05; 6·13 μ; λ_{max}^{MeOH} 256 mμ (ε, 14,000).

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