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ACID-CATALYSED REARRANGEMENTS OF 17β-ACETOXY-A-NOR-5α-ANDROSTAN-1α,2α-EPOXIDE

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Abstract—Reaction of 17β-acetoxy-A-nor-5α-androstan-1α,2α-epoxide (Ib) with acetic acid gave mainly the rearranged products IIIc, IVb and IVc, arising from C-19 Me migration, together with the unrearranged products IIa and IIb. Reaction of Ib with BF_3-etherate in ether afforded the rearranged products IIIb, IVb, XIIIb and XIVb, accompanied by a small amount of the fluorohydrin (XVb). Further, reaction of Ib with BF_3-etherate in benzene gave only the rearranged products IIIb, IVb, XIIIb, XIVb and XVIb. The structures of these rearranged products were established on the basis of chemical reactions and spectral data.

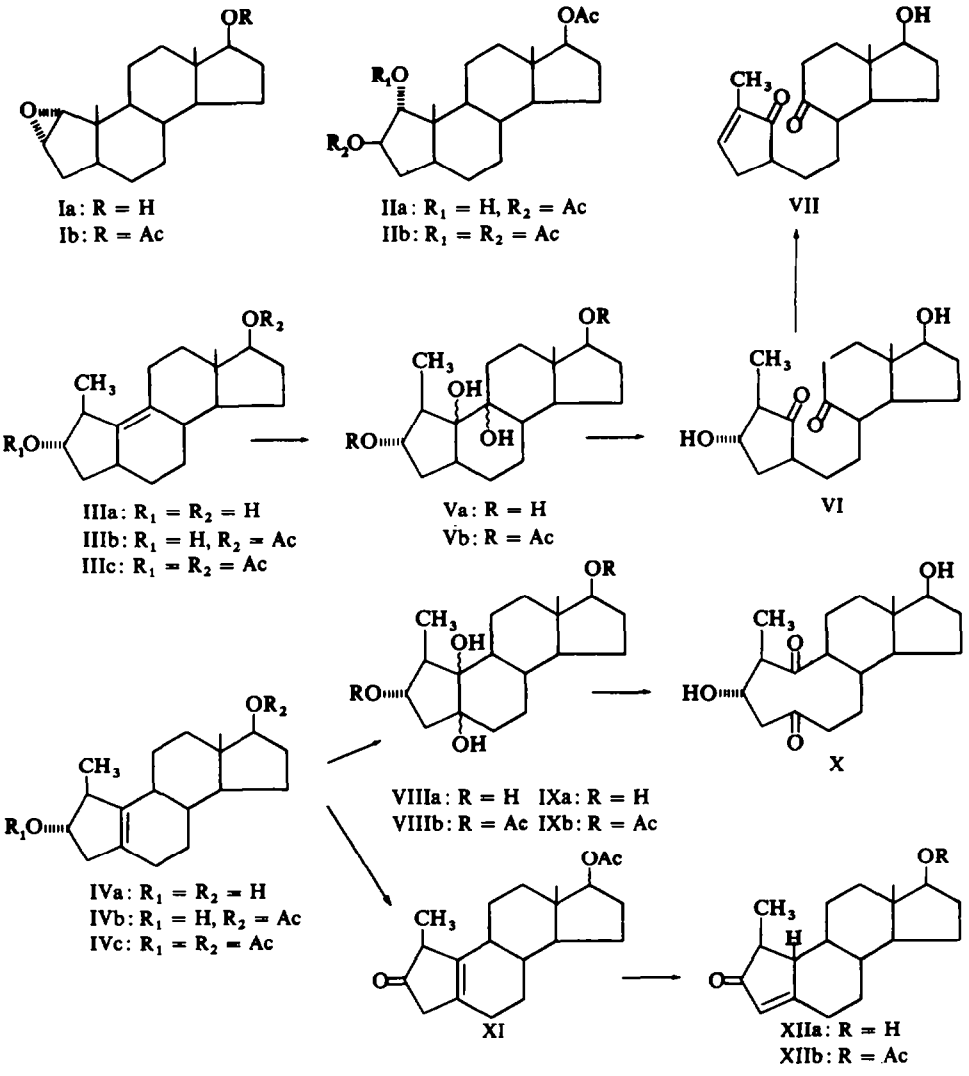
IT IS known that acid-catalysed ring cleavage of the steroidal tri-[1] and tetra-[2] substituted epoxides occasionally causes a Wagner–Meerwein type rearrangement involving angular Me migration. Regarding the di-substituted epoxide, however, few examples have been described. Kaufmann[3] isolated 1-methylestradiol diacetate on treatment of 17β-acetoxy-1α,2α-epoxy-5α-androstan-3-one with *p*-toluenesulfonic acid in acetic anhydride. Ganguly *et al.*[4] also found that reaction of the 4,4-dimethyl-1α,2α-epoxy-3-oxo compound with BF_3–etherate yielded the 1,4,4-trimethyl-2α-hydroxy-$\Delta^{1(10)}$-3-oxo compound. In the course of a preceding study,[5] it was found that the cleavage of 17β-acetoxy-A-nor-5α-androstan-1α,2α-epoxide[6] (Ib) with acetic acid yielded mainly C-19 Me migrated products. This paper deals with the Wagner–Meerwein type rearrangements of a disubstituted epoxide in the steroidal 5-membered ring with acetic acid and with BF_3–etherate.

Refluxing of Ib with glacial acetic acid for 7 hr and separation by TLC on silica gel affords an oily substance (55·5%) as the major product. A crystalline substance (6·3%), m.p. 158–161°, was obtained as the minor product together with the expected A-nor-5α-androstane-1α,2β,17β-triol 2,17-diacetate[5] (IIa, 15·2%) and its triacetate[5] (IIb, 6·6%). The oily substance appears as two spots in close proximity on TLC, and the IR spectrum displays OAc bands but no OH band. Alkali hydrolysis of this substance gives a crystalline material from which two diols, m.p. 228–231° and m.p. 158–162°, can be isolated in the ratio of 1:1 by fractional crystallization. The diols have the same molecular formula, $C_{18}H_{28}O_2$, and on acetylation give the respective diacetate as an oil. On the other hand, the crystalline substance obtained from chromatography has both OH and OAc bands in its IR spectrum, and on alkali hydrolysis gives the latter diol, m.p. 158–162°, and on acetylation its diacetate.

The NMR spectra of the diols exhibit doublets at 9·04 τ (J = 7·2 c/s) and 9·08 τ (J = 7·0 c/s) due to one Me, indicative of the secondary nature of the Me group. A positive tetranitromethane test, the absence of any olefinic proton signals in the

NMR spectrum and UV* absorption maxima at 220 mμ (ε 6,300) and 193 mμ (ε 7,100) reveal the presence of a tetra-substituted double bond in both diols. From the above results, it was found that rearrangement involving C-19 Me migration to C-1 had occurred, and thus the resultant diols must possess either a Δ^9- or $\Delta^{5(10)}$-1β-methyl-2α,17β-diol structure formulated as IIIa and IVa. In agreement with the assigned 2α-OH configuration for both diols, the NMR signals of the C-2 proton appear as a broad doublet at 6·07 τ (J = 3·0 c/s) in IIIa and at 6·17 τ (J = 4·6 c/s) in IVa, because the molecular models corresponding to structures IIIa and IVa indicate that the dihedral angles for the 2β-proton and the α-protons at C-1 and C-3 are close to 90°.

CHART 1



* The UV spectrum was obtained in an acetonitrile solution with a Beckman Model DK-2A Far UV Spectrophotometer.

Locations of the double bonds in these rearranged products are determined by the following reactions. Hydroxylation of IIIc with osmium tetroxide affords the single *cis*-glycol (Vb). Alkali hydrolysis of Vb gives the tetrol (Va), which is also obtained from the direct oxidation of IIIa with osmium tetroxide. Regeneration of Vb on acetylation of Va with acetic anhydride in pyridine shows that the inserted *cis*-glycol is located at tertiary carbons. Oxidative cleavage of Va with lead tetraacetate gives an oily diketone. The IR spectrum of the diketone displays bands at 1740 and 1706 cm^{-1}, characteristic of 5- and 6-membered ring ketones, respectively, and indicates that the diketone has the structure formulated as VI. The diketone (VI), possessing a β-hydroxy ketone structure, is readily dehydrated with base to give the α,β-unsaturated ketone (VII), m.p. 87–89°, λ_{max} 229 mμ (ε 9900). These facts indicate that the parent olefin must have the Δ^9-structure (IIIa).

In a similar way, hydroxylation of IVc with osmium tetroxide affords an equal amount of the epimeric *cis*-glycols VIIIb and IXb. Both *cis*-glycols on alkali hydrolysis give the corresponding tetrols VIIIa and IXa, which regenerate VIIIb and IXb by acetylation, respectively. As expected, oxidative cleavages of these isomeric tetrols with lead tetraacetate give the same diketone, m.p. 149–151°, $\nu_{max}^{CHCl_3}$ 3605, 3520, 1702, 1692 cm^{-1}, which is thought to be an A/B seco compound as in X. Based on these results, the parent olefin has the $\Delta^{5(10)}$-structure (IVa). The double bond positions being established, the original oily substance must be a mixture of the rearranged products IIIc and IVc, and the crystalline substance is IVb.

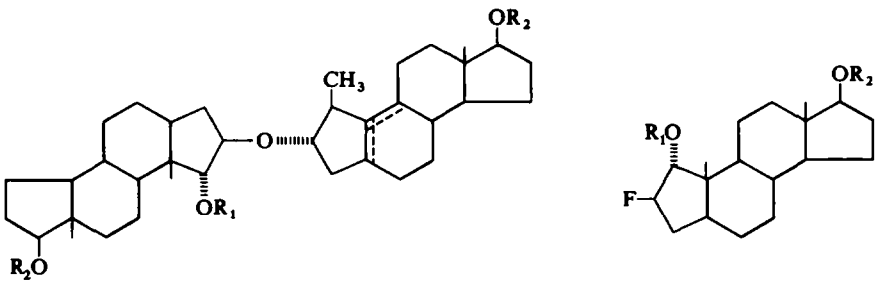
The mechanism for the formation of the rearranged products IIIc and IVc presumably involves cleavage of the C_1—O bond with the concerted migration of the 10β-Me group, subsequent loss of the axial 9α-H or 5α-H and the further acetylation of the primary products IIIb and IVb with glacial acetic acid. Actually, treatment of Ib with glacial acetic acid for 1 hr gives IIIb besides the above-mentioned products and its structure will be given later.

In order to obtain further confirmation of the structure (IVb), oxidation of the 2α-OH group was carried out using the Pfitzner–Moffatt technique.[7] Treatment of IVb with dicyclohexylcarbodiimide in dimethylsulfoxide containing a catalytic amount of pyridinium trifluoroacetate at room temperature affords the 2-ketone (XI) in a 46% yield. Refluxing of XI with a methanolic potassium carbonate solution gives a single conjugated ketone, m.p. 171–171·5°, λ_{max} 235 mμ (ε 17,600), which on acetylation yields the 17-acetate. Based on the following observations, this conjugated ketone is assigned as 17β-hydroxy-1β-methyl-A-norestr-3(5)-en-2-one (XIIa). The NMR spectrum of XIIa exhibits a doublet at 8·81 τ (J = 7·0 c/s) due to the C-1 Me, and a broad singlet at 4·19 τ due to the C-3 olefinic proton, as expected for a $\Delta^{3(5)}$-2-ketone structure. Further, ORD shows a negative Cotton curve similar to that of A-nortestosterone,[8] possessing a 10β-Me configuration. Assignment of the 1β-Me configuration is deduced from the fact[8] that the 1β-orientation in A-nortestosterone is thermodynamically stable from 1α-orientation.

In view of the above findings, the behaviour of the epoxide (Ib) towards BF_3 as an acid-catalyst was investigated. Treatment of Ib with BF_3-etherate in anhydrous ether at 5° for 2 hr affords a mixture of several products. The isolation of products from the mixture was accomplished by preparative TLC yielding four products.

The first and major product is a crystalline substance (27·8%) whose IR spectrum contains both OH and OAc bands. Although the substance appeared homogeneous

CHART 2



XIIIa: Δ^9, $R_1 = R_2 = H$
XIIIb: Δ^9, $R_1 = H$, $R_2 = Ac$
XIIIc: Δ^9, $R_1 = R_2 = Ac$

XIVa: $\Delta^{5(10)}$, $R_1 = R_2 = H$
XIVb: $\Delta^{5(10)}$, $R_1 = H$, $R_2 = Ac$
XIVc: $\Delta^{5(10)}$, $R_1 = R_2 = Ac$

XVa: $R_1 = R_2 = H$
XVb: $R_1 = H$, $R_2 = Ac$
XVc: $R_1 = R_2 = Ac$

on TLC examination, it is a mixture (NMR spectroscopy). The acetate prepared by usual acetylation can be separated by preparative TLC into two crystalline acetates, m.p. 133–143° and m.p. 153–158°, which have no OH bands in their IR spectra. Elementary analyses and molecular weight determinations show that these acetates are isomeric dimer triacetates of the same molecular formula, $C_{36}H_{53}O_4(COMe)_3$. Alkali hydrolysis of the triacetates yields the respective triols which, upon acetylation, regenerate the respective parent triacetates. The NMR spectrum of the former triacetate exhibits singlets at 9·22 τ (3H, 1Me), 9·13 τ (6H, 2Me), 7·98 τ (9H, 3COMe) and 5·22 τ (1H, 1 $>C<^{OAc}_{H}$), doublets at 9·01 τ (3H, J = 7·5 c/s, 1Me) and 6·23 τ (1H, J = 3·4 c/s, 1 $>C<^{O}_{H}$) and multiplets centered at 6·35 τ (1H, 1 $>C<^{O}_{H}$) and 5·42 τ (2H, 2 $>C<^{OAc}_{H}$). Similarly, the latter triacetate shows singlets at 9·22 τ (3H, 1Me), 9·19 τ (3H, 1Me), 9·14 τ (3H, 1Me), 7·97 τ (9H, 3COMe) and 5·20 τ (1H, τ (1H, 1 $>C<^{OAc}_{H}$), doublets at 8·93 τ (3H, J = 7·2 c/s, 1Me) and 6·17 τ (1H, J = 4·4 c/s, 1 $>C<^{O}_{H}$) and multiplets centered at 6·33 τ (1H, 1 $>C<^{O}_{H}$) and 5·40 τ (2H, 2 $>C<^{OAc}_{H}$). The above NMR spectral data indicate the following structural features for both dimers; one secondary and three tertiary Me groups, suggestive of an angular Me migration, three secondary OAc groups, one of which is thought to be situated at C-1 in vicinal substitutions at 1α and 2β and one ether bridge. A positive tetranitromethane test for each dimer indicates the presence of a double bond which is found to be a tetra-substituted olefin from the

absence of olefinic proton signals in NMR spectra. Further, UV spectra* exhibit absorption maxima at 218 mμ (ε 6700) in the former triacetate and 201 mμ (ε 6900) in the latter triacetate. Thus, the isomeric dimer triacetates are thought to be the unsymmetrical di-steroidal ethers formulated as XIIIc and XIVc, respectively, produced in a way similar to the formation of the di-steroidal ether reported by Kirk *et al.*[9]

The second and minor crystalline product from the above preparative TLC is the fluorohydrin (XVb, 5·3%), which is converted into the diol (XVa) by alkali hydrolysis and into the diacetate (XVc) by acetylation. Vigorous treatment of XVb with a methanolic potassium hydroxide solution yields the 1α,2α-epoxide[6] (Ia). Structural assignment of XVb follows from the NMR spectrum, which shows doublets at 9·18 τ (J = 1·8 c/s) and 6·13 τ (J = 14·4 c/s) due to the C-19 Me and 1β-H, respectively, which are coupled with the 2β-F atom.

The third product is an oily substance (9·7%) which on alkali hydrolysis gives IIIa and on acetylation IIIc. This substance has both OH and OAc bands in the IR spectrum and is thus defined as the Δ^9-1β-methyl-2α,17β-diol 17-acetate (IIIb). The compound IIIb is labile and cannot be oxidized by the method of Pfitzner–Moffatt.[7] The most polar crystalline product is the $\Delta^{5(10)}$-compound (IVb, 20·2%).

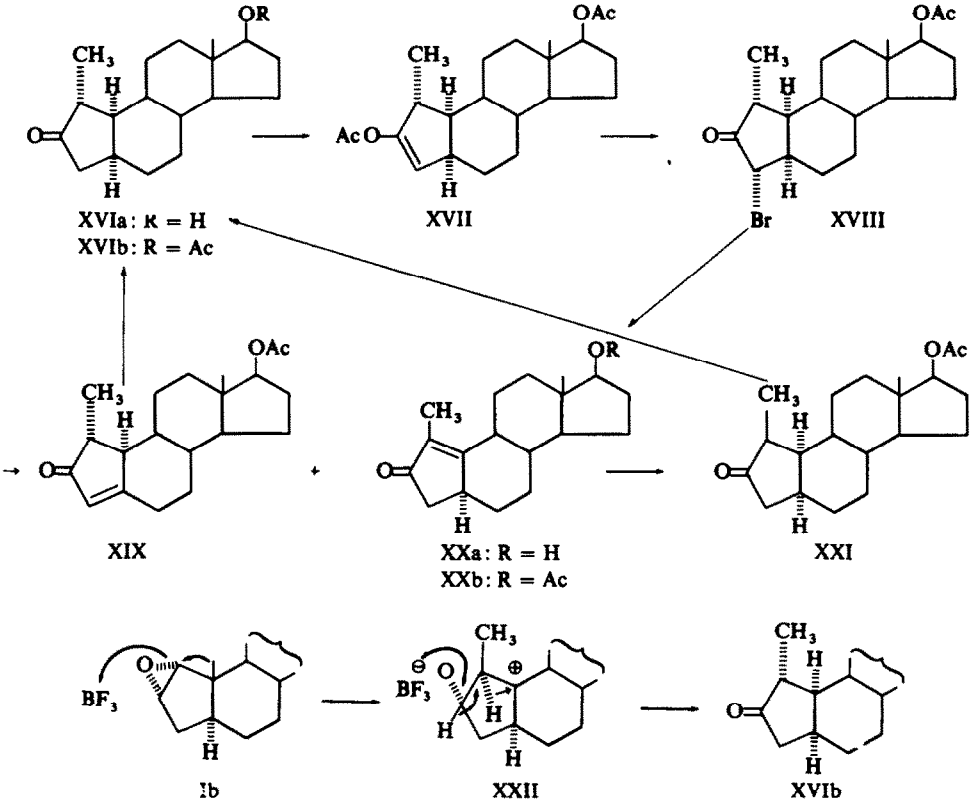
Finally, reaction of the epoxide (Ib) with BF_3-etherate was examined using a non-polar solvent, benzene, as the reaction solvent. The reaction in anhydrous benzene, unlike that in ether, rapidly colors and TLC examination shows that Ib is completely degraded within 10 min at 5°. Separation of the reaction mixture by preparative TLC affords five products. As minor products, the above dimer mixture (XIIIb and XIVb, 9%), the Δ^9-compound (IIIb, 8·8%) and the $\Delta^{5(10)}$-compound (IVb, 19%) were obtained. The major product in this reaction was a new OH-free solid (40%) having the formula $C_{20}H_{30}O_3$, m.p. 101–102°, shown below to have the structure XVIb: Hydrolysis of XVIb with a methanolic sodium hydroxide solution gives the 17β-ol (XVIa) which regenerates XVIb on usual acetylation. The IR spectrum of XVIa displays the band of a 5-membered ring ketone at 1743 cm^{-1} and the tetranitromethane test was negative, indicating a saturated compound. However, XVIa differs from known 17β-hydroxy-A-nor-5α-androstan-1-one[6] or -2-one[6], and is a rearranged product due to C-19 Me migration (NMR spectrum) in which one Me signal appears as a doublet at 8·82 τ (J = 6·0 c/s). The ORD curve of XVIa shows a negative Cotton effect (a −168) which suggests a 2-ketone structure possessing a 5α,10α-*cis* configuration, or a 1-ketone[6] in the 5α,10β-*trans* series. On the basis of these spectral data and on mechanistic considerations, the parent ketone is defined as 17β-acetoxy-1α-methyl-A-nor-5α,10α-estran-2-one (XVIb).

Migration of the C-19 Me group to C-1 with formation of a $\Delta^{1(10)}$-structure by a Wagner–Meerwein type rearrangement was reported[4,10] for the normal steroid series. In a similar way, the mechanism for the formation of XVIb is probably non-concerted and involves generation of a carbonium ion (XXII) at C-10 by cleavage of the C_1—O bond followed by the 10β-Me migration. Subsequent migration of the 1α-H to C-10 and in turn, the 2β-H to C-1, gives rise to the ketone (XVIb).

Chemical evidence for the assigned structure (XVIb) is provided by the following chemical transformations. Treatment of XVIb with isopropenyl acetate and a catalytic

* The UV spectrum was obtained in an acetonitrile solution with a Beckman Model DK-2A Far UV Spectrophotometer.

CHART 3



amount of sulfuric acid yields an oily enol acetate, for which the Δ^2-structure XVII is confirmed from the NMR spectrum, having a doublet for the C-1 Me signal and a multiplet for the C-3 olefinic proton. Treatment of XVII with one equivalent of bromine in CCl_4 affords the bromoketone (XVIII). The 3α-configuration of the Br atom introduced is confirmed by the following spectral data. In the NMR, the proton on the Br-bearing C atom appears as a broad singlet signal at 6·16 τ, suggesting a 3α-Br atom. The positive Cotton effect with an amplitude of +86 in the ORD supports the 3α-Br configuration, as a 3β-Br structure would be expected to give rise to a negative Cotton effect. Furthermore, compared with the parent ketone (XVIb), a red shift of 25 mμ in the UV for the CO absorptions indicates the quasi-axial nature of the 3α-bond, which is in good agreement with an inspection of the Dreiding model.

Treatment of XVIII with hydrogen bromide and acetic acid at room temperature results in dehydrobromination to give a conjugated ketone, m.p. 132–133°, λ_{max} 241·5 mμ (ε 16,500), as the sole product. This conjugated ketone was taken as the rearranged $\Delta^{1(10)}$-2-ketone (XXb) on the basis of the NMR spectrum, in which the C-1 Me signal appears as a broad singlet at 8·12 τ and no olefinic proton signal is observed. This behaviour of the bromoketone towards hydrogen bromide in acetic acid is consistent with results reported by House *et al.*[11] in the *cis*-decalone series. Dehydrobromination of XVIII with lithium carbonate in dimethylformamide affords

a mixture of the $\Delta^{3(5)}$-2-ketone (XIX), m.p. 161–164°, λ_{max} 239 mμ (ε 13,700), and the rearranged conjugated ketone (XXb). Location of the double bond between C-3 and C-5 in XIX is determined by the NMR with a doublet at 8·79 τ (J = 7·0 c/s) and a broad singlet at 4·15 τ due to the C-1 Me and the C-3 olefinic proton, respectively. In fact, XIX is readily hydrogenated with Pd–C to give XVIb as expected. On the other hand, hydrogenation of the $\Delta^{1(10)}$-2-ketone (XXb) with Adams' catalyst in methanol affords the 1β-methyl-2-ketone (XXI), m.p. 182–184°, accompanied by a small amount of the 1α-methyl-2-ketone (XVIb). The observed Cotton effect (a −88) allows the assignment of a 5α,10α-*cis*-configuration to XXI. Brief refluxing of XXI with a methanolic potassium carbonate solution results in complete isomerization into the stable isomeric 1α-methyl-2-ketone (XVIa). The lower stability of the 1β-Me isomer (XXI) to base probably lies in the structural feature of the *cis*-fused A/B ring bending to the β-side, in which the 1β-Me group would be expected to have a severe non-bonding interaction with the axial 8β-H and 11β-H. Thus, the structural correlation between the isomeric 1-methyl-2-ketones is established and the structure assigned to the parent ketone (XVIb) is shown to be correct.

As mentioned above, several rearranged products were isolated by treating the 1α,2α-epoxide (Ib) with acetic acid and with BF_3-etherate, but no products resulting from the backbone rearrangement[9, 12] of Ib were isolated.

EXPERIMENTAL

All m.ps were determined in capillary tubes and are uncorrected. Optical rotations were measured in dioxan solns at ca. 25° with a Perkin–Elmer Polarimeter type 141. Unless otherwise stated, IR spectra were recorded in Nujol mulls with a Nihon Bunko Infrared Spectrophotometer Model DS 201B, and UV spectra in 95% EtOH solns with a Hitachi EPS-2 Recording Spectrometer. NMR spectra were determined at 60 Mc in $CDCl_3$ solns containing TMS as an internal standard on a Varian A-60 Analytical NMR Spectrometer. ORD curves were run in MeOH solns at ca. 25° on a Nihon Bunko Automatic Recording Spectropolarimeter ORD/UV-5. For TLC, Merck Silica Gel G or GF_{254} was used. All solvent extracts were dried over anhyd Na_2SO_4.

Treatment of the 1α,2α-*epoxide* (Ib) *with acetic acid*

A soln of Ib[6] (4 g) in glacial AcOH (200 ml) was heated to reflux for 7 hr in a N_2 atom. After cooling, the soln was concentrated *in vacuo* and extracted with AcOEt. The extract was washed with 5% Na_2CO_3 and H_2O, dried and evaporated leaving a glassy residue which was chromatographed on silica gel (65 g, Merck, 0·2–0·5 mm). Elution with benzene gave an oily product (210 mg) which was unknown.

The next fraction eluted with benzene and benzene–$CHCl_3$ (8:2) was an unseparable oily mixture of the rearranged products (IIIc and IVc, 2·515 g, 55·5%), described in the next experiment.

The further fraction (1·86 g) eluted with benzene–$CHCl_3$ (1:1) and $CHCl_3$–MeOH (50:1) showed three spots on TLC and was separated by preparative TLC (benzene–AcOEt = 3:1). The most mobile fraction was IIb (349 mg, 6·6%). The more mobile fraction was IIa, (725 mg, 15·2%). These two acetates were described previously.[5] The less mobile fraction (254 mg, 6·3%) was twice recrystallized from acetone giving needles (53 mg) of IVb, m.p. 158–161°. $[\alpha]_D$ +31·6° (*c* 0·44); ν_{max} 3260, 1739, 1251 cm^{-1}; $\lambda_{max}^{CH_3CN^*}$ 194 mμ (shoulder) (ε 6700); NMR τ: 9·00 (3H, d, J = 7·0 c/s, C_1—Me), 6·10 (1H, d, J = 4·0 c/s, C_2—H). (Found: C, 75·55; H, 9·55. $C_{20}H_{30}O_3$ requires: C, 75·43; H, 9·50%).

1β-*Methyl-A-nor-5α-estr-9-ene-2α,17β-diol* (IIIa) *and the diacetate* (IIIc) *and* 1β-*methyl-A-norestr-5(10)-ene-2α,17β-diol* (IVa) *and the diacetate* (IVc)

A soln of the above mixture (2·515 g) of IIIc and IVc in 80% MeOH (200 ml) and K_2CO_3 (2·5 g) was refluxed for 30 min. The soln was extracted with AcOEt and the extract was washed with H_2O, dried and evaporated to dryness. Recrystallization of the crude product from acetone afforded square plates (400 mg) of IIIa, m.p. 228–231°. Concentration of the mother liquor gave the second crop (216 mg), m.p. 218–225°. The first crop showed the following constants: $[\alpha]_D$ +45·6° (*c* 0·51); ν_{max} 3290 cm^{-1}; $\lambda_{max}^{CH_3CN^*}$ 220 mμ

(ε 6300); NMR τ: 9·04 (3H, d, J = 7·2 c/s, C_1—Me), 6·07 (1H, d, J = 3·0 c/s, C_2—H). (Found: C, 78·30; H, 10·27. $C_{18}H_{28}O_2$ requires: C, 78·21; H, 10·21%).

The mother liquor of the second crop of IIIa was evaporated to give a semisolid residue (1·17 g) which was chromatographed on Al_2O_3 (40 g, Woelm, Act II). The fraction (900 mg) eluted with benzene and benzene–$CHCl_3$ (1:1) was twice recrystallized from acetone–n-hexane to give IVa (413 mg) as fine needles, m.p. 158–162°. Concentration of the mother liquor gave the second crop (237 mg), m.p. 152–160°, and the first crop showed the following constants: $[\alpha]_D$ +44·2° (*c* 0·47); ν_{max} 3330 cm^{-1}; $\lambda_{max}^{CH_3CN}$ 193 mμ (sh) (ε 7100); NMR τ: 9·08 (3H, d, J = 7·0 c/s, C_1—Me), 6·17 (1H, d, J = 4·6 c/s, C_2—H). (Found: C, 78·17; H, 10·22. $C_{18}H_{28}O_2$ requires: C, 78·21; H, 10·21%).

The fraction (67 mg) eluted with benzene–$CHCl_3$ (1:1) and $CHCl_3$ afforded, on recrystallization from acetone, an additional IIIa (29 mg), m.p. 223–228°.

A soln of IIIa (217 mg) in pyridine (2 ml) and Ac_2O (1 ml) was allowed to stand at room temp overnight. The product, isolated in the usual way, was an oily substance (283 mg) which was characterized as IIIc by the IR spectrum; $\nu_{max}^{CHCl_3}$ 1728 cm^{-1}.

Acetylation of IVa or IVb with Ac_2O and pyridine at room temp afforded the same oily diacetate (IVc), $\nu_{max}^{CHCl_3}$ 1730 cm^{-1}.

Hydrolysis of the $\Delta^{5(10)}$-2α.17β-*diol* 17-*acetate* (IVb)

A mixture of IVb (100 mg) in 80% MeOH (10 ml) and K_2CO_3 (100 mg) was refluxed for 30 min and extracted with AcOEt. The extract was washed with H_2O, dried and evaporated leaving a crystalline residue. Recrystallization from acetone–n-hexane gave fine needles (70 mg), m.p. 158–162°, identical with a sample of IVa described above by the mixed m.p. determination and IR comparison.

Hydroxylation of the diacetate (IIIc) *with osmium tetroxide*

To a soln of IIIc (283 mg) in ether (15 ml) containing 0·3 ml of pyridine, a soln of OsO_4 (240 mg) in ether (5 ml) was added. The soln was allowed to stand at room temp for 48 hr and poured into a large volume of pet. ether. The precipitated osmate was filtered off and dissolved in dioxan. A stream of H_2S was bubbled through the soln kept in an ice bath and the ppts were removed by filtration. The filtrate was evaporated to give a crystalline product which was purified by preparative TLC (benzene–AcOEt = 1:1). The main fraction (225 mg) was recrystallized from acetone–pet ether affording V_b (195 mg) as plates, m.p. 202–204°; $[\alpha]_D$ −34·5 (*c* 0·45); ν_{max} 3500, 1730, 1711, 1266, 1254 cm^{-1}; NMR τ: 8·63 (3H, d, J = 7·3 c/s, C_1—Me), 5·00 (1H, m, C_2—H). (Found: C, 67·20; H, 8·52. $C_{22}H_{34}O_6$ requires: C, 66·98; H, 8·69%).

1β-*Methyl-A-nor*-5α-*estrane*-2α,9ξ,10ξ,17β-*tetrol* (Va)

(a) *From the diol* (IIIa). To a soln of IIIa (400 mg) in pyridine (15 ml) was added OsO_4 (442 mg) and the soln was kept at room temp for 24 hr. The crude product, isolated in the same manner as described in the preceding experiment, was purified by preparative TLC (benzene–MeOH = 3:1). Recrystallization of the main fraction from acetone afforded Va (240 mg) as plates, m.p. 170–172°; $[\alpha]_D$ −15·5° (*c* 0·58). ν_{max} 3350 cm^{-1}. (Found: C, 69·39; H, 9·74. $C_{18}H_{30}O_4$ requires: C, 69·64; H, 9·74%).

(b) *By hydrolysis of* Vb. A mixture of Vb (210 mg) in 80% MeOH (30 ml) and K_2CO_3 (300 mg) was refluxed for 1 hr. After dilution with AcOEt, the organic soln was washed with H_2O, dried and evaporated leaving a crystalline residue. Recrystallization from acetone gave plates (125 mg), m.p. 170–172°, identical with a sample of Va obtained in (a).

Acetylation of Va with Ac_2O in pyridine at room temp overnight gave back Vb.

Hydroxylation of the diacetate (IVc) *with osmium tetroxide*

To a soln of IVc (290 mg) in ether (15 ml) containing 0·3 ml of pyridine, a soln of OsO_4 (246 mg) in ether (5 ml) was added. The soln was allowed to stand at room temp for 24 hr and poured into a large volume of pet ether. The precipitated osmate was filtered off and dissolved in dioxan. A stream of H_2S was bubbled through the soln kept in an ice bath. After removal of the ppts by filtration, the filtrate was evaporated leaving a residue which was separated by preparative TLC (benzene–AcOEt = 1:1) into two fractions. The upper fraction (68 mg) was an oily substance which was characterized as VIIIb by the IR spectrum, $\nu_{max}^{CHCl_3}$ 3540, 1730 cm^{-1}.

The lower fraction (68 mg) was recrystallized from acetone–pet ether giving plates (49 mg) of the isomeric

IXb, m.p. 156–159°; $[\alpha]_D$ −17·5° (*c* 0·58); $\nu_{max}^{CHCl_3}$ 3520, 1727 cm^{-1}. (Found: C, 65·43; H, 8·69. $C_{22}H_{34}O_6 \cdot \frac{1}{2} H_2O$ requires: C, 65·48; H, 8·74%).

Isomeric 1β-*methyl-A-norestrane-*2α,5ξ,10ξ,17β-*tetrols*, (VIIIa) *and* (IXa)

(a) A mixture of the foregoing oily fraction (68 mg) of VIIIb in 80% MeOH (13 ml) and K_2CO_3 (130 mg) was refluxed for 1 hr and extracted with AcOEt. The extract was washed with H_2O, dried and evaporated to dryness. Recrystallization of the product from acetone afforded VIIIa as square plates, m.p. 234–236°; $[\alpha]_D$ +21·5° (*c* 0·56); ν_{max} 3480, 3330 cm^{-1}. (Found: C, 69·66; H, 9·87. $C_{18}H_{30}O_4$ requires: C, 69·64; H, 9·74%).

(b) A mixture of IXb (m.p. 156–149°) in 80% MeOH and K_2CO_3 was refluxed for 1 hr. Recrystallization of the product, isolated in the same manner as above, from acetone gave the isomeric IXa as fine plates, m.p. 217–220°, $[\alpha]_D$ −8·6° (*c* 0·53); ν_{max} 3420, 3290 cm^{-1}. (Found: C, 69·66; H, 9·76. $C_{18}H_{30}O_4$ requires: C, 69·64; H, 9·74%).

Acetylation of VIIIa and IXa with Ac_2O and pyridine in the usual way gave back the diacetates, VIIIb and IXb, respectively.

Oxidative cleavage of the tetrol (Va) *with lead tetraacetate*

To a soln of Va (155 mg) in $CHCl_3$ (40 ml) was added $Pb(OAc)_4$ (267 mg) with stirring at room temp and the mixture was stirred for an additional 1 hr. The soln was diluted with $CHCl_3$, washed with H_2O and dried. Removal of the solvent afforded an oily substance (108 mg), which was characterized as VI by the IR spectrum; $\nu_{max}^{CHCl_3}$ 3560, 3400, 1740 (5-membered ring ketone), 1706 (6-membered ring ketone) cm^{-1}.

Dehydration of the diketone (VI)

A soln of VI (30 mg) in MeOH (9 ml) containing 0·1N NaOH (6 ml) was allowed to stand at room temp for 1 hr under N_2 and extracted with AcOEt. The extract was washed with H_2O, dried and evaporated to dryness. After purification of the crude product by preparative TLC (benzene–AcOEt = 1:1), recrystallization from acetone–pet ether gave the conjugated ketone (VII) as plates, m.p. 87–89°; $[\alpha]_D$ +45·9° (*c* 0·99); $\nu_{max}^{CHCl_3}$ 3590, 3460, 1700, 1640 cm^{-1}; λ_{max} 229 mμ (ε 9900). NMR τ: 8·28 (3H, d, *J* = 1·6 c/s, C_1—Me), 2·77 (1H, m, C_2—H). (Found: C, 70·34; H, 9·08. $C_{18}H_{26}O_3 \cdot H_2O$ requires: C, 70·10; H, 9·15%).

Oxidative cleavage of the tetrol (VIIIa) *with lead tetraacetate*

To a soln of VIIIa (m.p. 234–236°, 99 mg) in $CHCl_3$ (40 ml) and MeOH (4 ml), $Pb(OAc)_4$ (170 mg) was added with stirring at room temp and the mixture was stirred for an additional 1 hr. The soln was diluted with $CHCl_3$, washed with H_2O, dried and evaporated to dryness. Recrystallization of the product (75 mg) from acetone–pet ether afforded plates (50 mg) of X, m.p. 149–151°; $[\alpha]_D$ −86·3° (*c* 0·50); $\nu_{max}^{CHCl_3}$ 3605, 3520, 1702, 1692 (shoulder) cm^{-1}. (Found: C, 69·97; H, 9·19. $C_{18}H_{28}O_4$ requires: C, 70·10; H, 9·15%).

Oxidative cleavage of the isomeric tetrol (IXa) *with lead tetraacetate*

Treatment of IXa (m.p. 217–220°, 25 mg) in $CHCl_3$ (10 ml) and MeOH (1 ml) with $Pb(OAc)_4$ (43 mg) was carried out in a manner similar to that described above. Recrystallization of the product (20 mg) from acetone–pet ether afforded plates (12 mg) of X, m.p. 149–151°, identical with a sample obtained in the above experiment.

17β-*Acetoxy-*1β-*methyl-A-norestr-*5(10)-*en-*2-*one* (XI)

According to the procedure of Moffatt,[7] IVb (460 mg) was dissolved in anhyd DMSO (5 ml) and benzene (2 ml) containing pyridinium trifluoroacetate (140 mg). After addition dicyclohexylcarbodiimide (894 mg), the mixture was kept at room temp for 24 hr and diluted with AcOEt. The precipitated dicyclohexylurea was removed by filtration and the filtrate was washed with 5% Na_2CO_3 and H_2O and dried. Removal of the solvent gave a semisolid residue which was separated by preparative TLC (benzene–AcOEt = 10:1). The crystalline fraction (337 mg) of a ketone was recrystallized from MeOH to give plates (211 mg) of XI, m.p. 107–109°; $[\alpha]_D$ +13·2° (*c* 0·55); $\nu_{max}^{CCl_4}$ 1750, 1245 cm^{-1}; NMR τ: 8·77 (3H, d, *J* = 7·2 c/s, C_1—Me). (Found: C, 75·61; H, 8·90. $C_{20}H_{28}O_3$ requires: C, 75·91; H, 8·92%).

17β-*Hydroxy-*1β-*methyl-A-norestr-*3(5)-*en-*2-*one* (XIIa) *and the acetate* (XIIb)

A mixture of XI (120 mg) in 80% MeOH (12 ml) and K_2CO_3 (120 mg) was refluxed for 30 min in a N_2 atm. The soln was extracted with AcOEt and the extract was washed with H_2O, dried and evaporated to

dryness. Recrystallization of the product from acetone afforded XIIa (68 mg) as needles, m.p. 169–171°; $[\alpha]_D$ −87·2° (*c* 0·51); $\nu_{max}^{CHCl_3}$ 3600, 1690, 1625, 865 cm^{-1}; λ_{max} 235 mμ (ε 17,600); NMR τ: 8·81 (3H, d, *J* = 7·0 c/s, C_1—Me), 4·19 (1H, broad s, C_3—H). ORD (*c* 0·508, dioxan): $[\phi]_{400}$ −1135, $[\phi]_{353}$ −4051, $[\phi]_{345}$ −3350, $[\phi]_{338}$ −3782, $[\phi]_{326}$ −756, $[\phi]_{311}$ +2150, $[\phi]_{300}$ + 3301, $[\phi]_{260}$ 0. (Found: C, 78·76; H, 9·56. $C_{18}H_{24}O_2$ requires: C, 78·79; H, 9·55%).

A soln of XIIa (35 mg) in pyridine (1 ml) and Ac_2O (0·5 ml) was allowed to stand at room temp overnight. The product was recrystallized from n-hexane to yield XIIb (29 mg) as fine needles, m.p. 105–106°; $[\alpha]_D$ −77·6° (*c* 0·54); $\nu_{max}^{CHCl_3}$ 1725, 1690, 1625, 866 cm^{-1}; λ_{max} 234·5 mμ (ε 14,700). (Found: C, 75·87; H, H, 8·90. $C_{20}H_{28}O_9$ requires: C, 75·91; H, 8·92%).

Treatment of the 1α,2α*-epoxide* (Ib) *with* BF_3 *in ether*

To a soln of Ib (750 mg) in anhyd ether (30 mg) kept in an ice bath was added BF_3–etherate (0·75 ml) and the soln was kept at 5° for 2 hr. The soln was diluted with ether, washed with 5% Na_2CO_3 and H_2O and dried. Evaporation of the solvent *in vacuo* gave a glassy residue which was separated by preparative TLC (benzene–AcOEt = 3:1) into five fractions. The non polar fraction was an oil (240 mg) which showed again several spots on TLC and was not detected.

The less polar fraction (209 mg, 27·8%) was crystallized from MeOH to give the dimer mixture (XIIIb and XIVb), m.p. 150–153°, ν_{max} 3530, 1741, 1722, 1279, 1250 cm^{-1}, which is described in the next experiment.

The next polar fraction (42 mg, 5·3%) was recrystallized from acetone–pet ether to give XVb (23 mg) as needles, m.p. 185–186°; $[\alpha]_D$ +17·5 (*c* 0·44); ν_{max} 3485, 1715, 1267 cm^{-1}; NMR τ: 9·18 (3H, d, *J* = 1·8 c/s. C_{19}—Me), 6·13 (1H, d, *J* = 14·4 c/s, C_1—H). (Found: C, 71·16; H, 9·48. $C_{20}H_{31}O_3F$ requires: C, 70·99; H, 9·23%).

The more polar fraction was an oily product (73 mg, 9·7%) which was characterized as IIIb by the following reactions and IR spectrum; $\nu_{max}^{CHCl_3}$ 3600, 1725 cm^{-1}. A mixture of IIIb in MeOH and K_2CO_3 was refluxed for 30 min and the product, isolated in the usual way, was recrystallized from acetone giving plates of IIIa, m.p. 228–231°. Identity with an authentic sample was established by the IR comparison and mixed m.p. determination. Acetylation of IIIb with Ac_2O in pyridine at room temp overnight afforded an oil, identical with a sample of IIIc by the IR comparison.

The most polar fraction (152 mg, 20·2%) afforded, on recrystallization from acetone, needles (135 mg), m.p. 158–161°, which was identified with a sample of IVb by the mixed m.p. determination and IR comparison.

The dimer triacetates, (XIIIc) *and* (XIVc)

A soln of the dimer mixture (209 mg), described in the preceding experiment, in pyridine (2 ml) and Ac_2O (1 ml) was allowed to stand at room temp overnight. The product, isolated in the usual way, showed two spots close together on TLC and was separated by preparative TLC (benzene-AcOEt = 10:1).

The more mobile fraction (75 mg) was recrystallized from MeOH to yield needles (65 mg) of XIIIc, m.p. 133–143°; $[\alpha]_D$ +20·0° (*c* 0·95); ν_{max} 1740, 1725, 1248 cm^{-1}; $\lambda_{max}^{CH_3CN}$ 218 mμ (ε 6700). (Found: C, 74·47; H, 9·25, mol. wt., 657. $C_{42}H_{62}O_7$ requires: C, 74·30; H, 9·21%, mol. wt., 679).

The less mobile fraction (97 mg) gave, on recrystallization from MeOH, XIVc (77 mg) as needles, m.p. 153–158°; $[\alpha]_D$ +22·3° (*c* 0·95); ν_{max} 1745, 1734, 1247 cm^{-1}; $\lambda_{max}^{CH_3CN}$ 201 mμ (shoulder) (ε 6900). (Found: C, 73·35; H, 9·10; mol. wt., 680. $C_{42}H_{62}O_7 \cdot \frac{1}{2}H_2O$ requires: C, 73·32; H, 9·23%, mol. wt., 688).

The dimer triol (XIIIa)

A mixture of XIIIc (116 mg) in 80% MeOH (24 ml) and K_2CO_3 (240 mg) was refluxed for 1 hr. After extraction with AcOEt, the extract was washed with H_2O, dried and evaporated to dryness. The crude product was purified by preparative TLC (benzene–AcOEt = 1:1) and recrystallization of the major fraction from acetone afforded plates (68 mg) of XIIIa, m.p. 151–160°; $[\alpha]$ +39·1° (*c* 0·60); ν_{max} 3420 cm^{-1}, $\lambda_{max}^{CH_3CN}$ 220 mμ (ε 6500). (Found: C, 77·93; H, 10·08. $C_{36}H_{56}O_4$ requires: C, 78·21; H, 10·21%).

Acetylation of XIIIa with Ac_2O and pyridine in the usual way regenerated the starting triacetate (XIIIc).

The dimer triol (XIVa)

Treatment of XIVc (110 mg) with 80% MeOH (22 ml) and K_2CO_3 (220 mg) was carried out in a manner similar to that described in the preceding experiment. Recrystallization of the product from MeOH gave

XIVa (45 mg) as fine needles, m.p. 186·190°; $[\alpha]_D$ +38·9° (*c* 0·51); ν_{max} 3380 cm^{-1}; $\lambda_{max}^{CH_3CN}$ 200 mμ (shoulder) (ε 6500). (Found: C, 76·88; H, 9·98. $C_{36}H_{56}O_4 \cdot \frac{1}{2}H_2O$ requires: C, 76·96; H, 10·23%).

Acetylation of XIVa with Ac_2O and pyridine in the usual way regenerated the starting XIVc.

Treatment of the fluorohydrin (XVb) *with base*

(a) *With potassium carbonate.* A mixture of XVb (34 mg) in 80% MeOH (5 ml) and K_2CO_3 (50 mg) was refluxed for 1 hr. After extraction with AcOEt, the organic soln was washed with H_2O, dried and evaporated to dryness. Recrystallization of the product from acetone–pet ether gave needles (18 mg) of XVa, m.p. 187–189°; $[\alpha]_D$ +26·0° (*c* 0·52); ν_{max} 3445 cm^{-1}. (Found: C, 72·69; H, 9·96. $C_{18}H_{29}O_2F$ requires: C, 72·93; H, 9·86%).

(b) *With potassium hydroxide.* A mixture of XVb (24 mg) in MeOH (5 ml) and KOH (50 mg) was heated to reflux during 4 hr under N_2. The soln was extracted with AcOEt and the extract was washed with H_2O, dried and evaporated to dryness. Recrystallization of the product from MeOH gave Ia (10 mg) as prisms, m.p. 177–179°, identical with an authentic sample[6] in all respects.

2β-*Fluoro-A-nor-5α-androstane*-1α,17β-*diol diacetate* (XVc)

Acetylation of XVb (50 mg) with pyridine (1 ml) and Ac_2O (0·5 ml) gave XVc (30 mg) as plates, m.p. 115–116°; $[\alpha]_D$ +5·5° (*c* 0·47); ν_{max} 1745 (sh), 1737, 1255, 1235 cm^{-1}. (Found: C, 69·67; H, 8·98. $C_{22}H_{33}O_4F$ requires: C, 69·44; H, 8·74%).

Treatment of the 1α,2α-*epoxide* (Ib) *with* BF_3 *in benzene*

To a soln of Ib (1·42 g) in anhyd benzene (28 ml), BF_3–etherate (1·4 ml) was added at 5° and the soln was kept at 5° for 10 min. The soln was diluted with benzene, washed with 5% Na_2CO_3 and H_2O and dried. Removal of the solvent gave a glassy residue which was separated by preparative TLC (benzene–AcOEt = 10:1) into five fractions. The least polar fraction was an oil (152 mg), the structure of which was unknown.

The less polar fraction (569 mg, 40%) was recrystallized from n-hexane to give needles (500 mg) of XVIb, m.p. 89–95°. Further recrystallization from n-hexane raised the m.p. to 101–102°; $[\alpha]_D$ −107·5° (*c* 0·49); $\nu_{max}^{CS_2}$ 1739, 1248 cm^{-1}; λ_{max} 294 mμ (ε 37) NMR τ: 8·82 (3H, d, *J* = 6·0 c/s, C_1—Me); ORD (*c* 0·03566); $[\phi]_{400}$ −1000, $[\phi]_{320}$ −7189, $[\phi]_{315}$ −7144, $[\phi]_{310·5}$ −7599, $[\phi]_{296}$ 0, $[\phi]_{276}$ +6081, $[\phi]_{230}$ +2456. (Found: C, 75·35; H, 9·66. $C_{20}H_{30}O_3$ requires: C, 75·43; H, 9·50%).

The more polar fraction was the aforementioned dimer mixture (XIIIb and XIVb, 128 mg, 9%), m.p. 150–153°. The next polar fraction was an oil (125 mg, 8·8%), whose IR spectrum was superimposable upon the spectrum of IIIb prepared by BF_3 treatment of Ib in ether.

The most polar fraction (270 mg, 19%) gave, on recrystallization from acetone, needles (192 mg) of IVb, m.p. 158–161°, identical with an authentic sample in all respects.

17β-*Hydroxy*-1α-*methyl-A-nor*-5α,10α-*estran*-2-*one* (XVIa)

A soln of XVIb (100 mg) in MeOH (9 ml) and 10% NaOH (1 ml) was heated to reflux for 1 hr. The soln was extracted with AcOEt and the organic soln was washed with H_2O and dried. Removal of the solvent and recrystallization of the product from n-hexane gave needles (73 mg) of XVIa, m.p. 122–123°; $[\alpha]_D$ −104·9° (*c* 0·96); $\nu_{max}^{CCl_4}$ 3610, 3450, 1743 cm^{-1}; NMR τ: 8·82 (3H, d, *J* = 6·0 c/s, C_1—Me); ORD (*c* 0·0391): $[\phi]_{400}$ −745, $[\phi]_{320}$ −7819, $[\phi]_{311}$ −8246, $[\phi]_{276}$ +8541, $[\phi]_{230}$ +4278. (Found: C, 78·27; H, 10·18. $C_{18}H_{28}O_2$ requires: C, 78·21; H, 10·21%).

Acetylation of XVIa (100 mg) with Ac_2O (1 ml) and pyridine (2 ml) at room temp overnight yielded, following the usual work-up, needles (93 mg), m.p. 100–102°, which was identified with a sample of the starting acetate (XVIb) by a mixed m.p. determination and the IR comparison.

2,17β-*Diacetoxy*-1α-*methyl-A-nor*-5α,10α-*estr*-2-*ene* (XVII)

To a soln of XVIb (500 mg) in isopropenyl acetate (20 ml), 0·5 ml of the catalyst soln (5 ml of isopropenyl acetate and 0·1 ml of conc H_2SO_4) was added and approximately 10 ml of the solvent was distilled over a period of 2 hr. The soln was extracted with pet ether and the extract was washed with 5% Na_2CO_3 and H_2O, dried and evaporated to dryness.

Purification of the glassy residue by preparative TLC (benzene) gave an oily product (478 mg) which was characterized as XVII by the IR and NMR spectra; $\nu_{max}^{CCl_4}$ 1760, 1740, 1663, 1640, 1248, 1213 cm^{-1}; NMR τ: 8·95 (3H, d, *J* = 6·6 c/s, C_1—Me), 4·48 (1H, m, C_3—H).

17β-Acetoxy-3α-bromo-1α-methyl-A-nor-5α,10α-estran-2-one (XVIII)

To a soln of XVII (478 mg) in CCl_4 (40 ml), a soln of Br_2 (212 mg) in CCl_4 (5 ml) was added dropwise with stirring at −10° and the soln was stirred for an additional 20 min. Removal of the solvent *in vacuo* below 40° afforded a crystalline residue which was purified by preparative TLC (benzene–AcOEt = 15:1). The main fraction was recyrstallized from MeOH yielding square plates (323 mg) of XVIII, m.p. 128° (dec); $[\alpha]_D$ +69·3° (*c* 0·53); $\nu_{max}^{CS_2}$ 1743, 1246 cm^{-1}; λ_{max} 319 mμ (ε 143); NMR τ: 8·60 (3H, d, J = 6·6 c/s, C_1—Me), 6·16 (1H, broad s, C_3—H); ORD (*c* 0·0232): $[\phi]_{400}$ +1200, $[\phi]_{340}$ +4282, $[\phi]_{293}$ −4282, $[\phi]_{252}$ −3940, $[\phi]_{233}$ 0. (Found: C, 60·45; H, 7·46; Br, 20·15. $C_{20}H_{29}O_3Br$ requires: C, 60·45; H, 7·36; Br, 20·11%).

Treatment of the bromoketone (XVIII) *with hydrogen bromide in acetic acid*

A mixture of XVIII (285 mg) in AcOH (25 ml) and 47% HBr (1·5 ml) was allowed to stand at room temp overnight. After dilution with AcOEt, the organic soln was washed with 5% Na_2CO_3 and H_2O, dried and evaporated to dryness. Recrystallization of the product from acetone–pet ether afforded plates (88 mg) of XXb, m.p. 129–131°.

The mother liquor was purified by preparative TLC (benzene–AcOEt = 7:1) to give an additional XXb (77 mg) as plates, m.p. 129–131°. Further recrystallization from the same solvent gave the analytical sample of XXb with following constants: m.p. 132–133°; [α] −144·5° (*c* 0·53); $\nu_{max}^{CCl_4}$ 1742, 1704, 1637, 1246 cm^{-1}; λ_{max} 241·5 mμ (ε 16,500); NMR τ: 8·12 (3H, broad s, C_1—Me). (Found: C, 75·68; H, 8·94. $C_{20}H_{28}O_3$ requires: C, 75·91; H, 8·92%).

17β-Hydroxy-1-methyl-A-nor-5α-estr-1(10)-en-2-one (XXa)

A mixture of XXb (41 mg) in 80% MeOH (8 ml) and K_2CO_3 (80 mg) was refluxed for 30 min in an N_2 atm. The product, isolated in the usual way, was recrystallized from acetone–pet ether yielding plates (29 mg) of XXa, m.p. 165–166°. $[\alpha]_D$ −142·7° (*c* 0·55); ν_{max} 3470, 1682, 1628 cm^{-1}; λ_{max} 243 mμ (ε 17,600). (Found: C, 78·81; H, 9·47. $C_{18}H_{26}O_2$ requires: C, 78·79; H, 9·55%).

Treatment of the bromoketone (XVIII) *with lithium carbonate in dimethylformamide*

A mixture of XVIII (220 mg) in DMFA (10 ml) and Li_2CO_3 (440 mg) was heated to reflux during 4 hr in a N_2 atm. After cooling, the mixture was extracted with AcOEt and the extract was washed with 5% HCl, 5% Na_2CO_3 and H_2O, dried and evaporated *in vacuo* to dryness. The product was purified by preparative TLC (benzene–AcOEt = 5:1) to give a crystalline fraction (155 mg). Recrystallization from acetone–pet ether gave plates (69 mg), m.p. 141–155°. Further recrystallization from the same solvent gave XIX m.p. 161–164°. $[\alpha]_D$ +1·3° (*c* 0·53); $\nu_{max}^{CCl_4}$ 1739, 1711, 1630, 1246, 869 cm^{-1}; λ_{max} 239 mμ (ε 13,700); NMR τ: 8·79 (3H, d, J = 7·0 c/s, C_1—Me), 4·15 (1H, broad s, C_3—H). (Found: C, 75·85; H, 8·87. $C_{20}H_{28}O_3$ requires: C, 75·91; H, 8·92%).

The mother liquor of XIX was concentrated to give another crystals (65 mg), m.p. 121–130°. Recrystallization from acetone–pet ether afforded plates, m.p. 129–131°, identical with a sample of XXb by a mixed m.p. determination and the IR comparison.

Hydrogenation of the conjugated ketone (XXb) *with Adams' catalyst*

A soln of XXb (94 mg) in MeOH (10 ml) was shaken with Adams' catalyst (50 mg) in an atm of H_2 for 6 hr. The catalyst was removed by filtration and the filtrate was evaporated to give a glassy residue which was separated by preparative TLC (benzene–AcOEt = 10:1) into three fractions. The most mobile fraction (11 mg) was recrystallized from n-hexane affording needles (7 mg), m.p. 97–100°, identical with a sample of XVIb by the mixed m.p. determination and the IR comparison.

The more mobile fraction (41 mg) gave, on recrystallization from n-hexane, XXI (32 mg) as plates, m.p. 180–182°; $[\alpha]_D$ −129·4° (*c* 0·52); $\nu_{max}^{CCl_4}$ 1742, 1250 cm^{-1}; NMR τ: 8·68 (3H, d, J = 6·8 c/s, C_1—Me); ORD (*c*, 0·03028): $[\phi]_{400}$ −1261, $[\phi]_{322}$ −5468, $[\phi]_{313·5}$ −6099, $[\phi]_{305}$ −3996, $[\phi]_{278}$ +2734, $[\phi]_{250}$ 0. (Found: C, 75·36; H, 9·46. $C_{20}H_{30}O_3$ requires: C, 75·43; H, 9·50%).

The less mobile fraction (34 mg) was recrystallized from acetone–pet ether giving plates (26 mg) of the unchanged starting ketone (XXb).

Hydrogenation of the conjugated ketone (XIX) *with palladium-on-charcoal*

A soln of XIX (32 mg) in MeOH (5 ml) was shaken with 5% Pd–C (80 mg) in an atm of H_2 for 20 min. After removal of the catalyst by filtration, the filtrate was evaporated to dryness. Recrystallization of the

product from n-hexane gave XVIb (24 mg) as needles, m.p. 98–100°, which was identical with an authentic sample by a mixed m.p. determination and the IR comparison.

Isomerization of the 1β-*methyl-2-one* (XXI) *with base*

A mixture of XXI (34 mg) in 80% MeOH (5 ml) and K_2CO_3 (50 mg) was refluxed for 30 min and the soln was extracted with AcOEt. The extract was washed with H_2O, dried and evaporated to dryness. Recrystallization of the product from n-hexane gave XVIa (25 mg) as needles, m.p. 122–123°. Identity with an authentic sample was established by the IR comparison and a mixed m.p. determination.

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