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THE SYNTHESIS OF ETIOJERVANE ANALOGUES OF CORTISONE*

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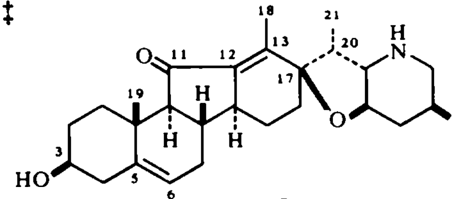
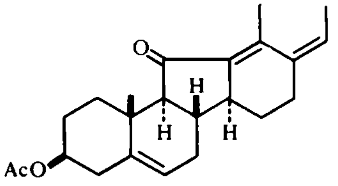
Abstract—The syntheses of C-nor-D-homo-cortisone 21-acetates (XIX and XVI), one of which possesses the cortisone configuration at each of the ring junctions has been described. Treatment of etiojerv-5-en-3β-ol-3,11-dione (III), obtained by degradation of jervine (I), with ethynylmagnesium bromide yielded stereoisomeric 17-ethynylcarbinols VII and VIII. Spectral and chemical studies show that (i) both the compounds possess C/D-*trans* and 13β-Me configurations and (ii) the 17-ethynyl group is oriented β in VII and α in VIII. Partial hydrogenation of VII in the presence of Lindlar catalyst gave rise to 17-vinylcarbinol XI, which on Oppenauer oxidation was converted into Δ^4-3-ketone XIII. Compound XIII was then derived, by oxidation with osmium tetroxide followed by partial acetylation, into C/D *trans*- and C/D *cis*-fused 20,21-glycol 21-acetates XIV' and XIV, although the former was not isolated in pure state. Oxidation of the acetates with Jones reagent led to formation of XIX and XVI. The configurational assignments for both compounds are based on spectral and chemical evidence.

IN THE past decade considerable attention has been paid to the synthesis of modified steroid hormones in search of analogues with enhanced or more specific physiological properties. In view of the natural occurrence of the C-nor-D-homosteroid ring system,[2] the synthesis of the hormone analogues[2b, 3–6] was undertaken. Etiojervane† analogs of testosterone,[3b, 4a, 5b] progesterone,[3, 4c] etc., have recently been prepared, using jervine or hecogenin as the starting materials. In the present paper we describe the synthesis of C-nor-D-homocortisone derivatives, one of which possesses the cortisone configuration at each of the ring junctions.

Jervine[8] (I), one of the most readily available veratrum alkaloids, was selected as the starting material for our investigation. An attempted synthetic approach to C-nor-D-homocortisone starting with 17-ethyletiojerva-5,12,17(20)-trien-3β-ol-11-one 3-acetate[9, 4a] (II), a nitrogen-free compound obtained by degradation of I, proved to be unsuccessful,[3a, 4b] although the ethylidene moiety of II appeared to be suitable for construction of a 17-side chain of cortisone. Thus it was deemed effective to introduce an appropriate side chain to C_{17} of etiojerv-4-en-3β-ol-11,17-dione[9a] (III).‡



I



II

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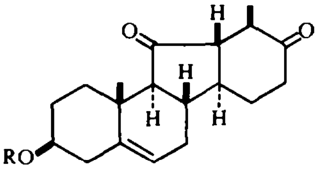
[*] Part XIII of *C-Nor-D-homosteroids and Related Alkaloids*; Part XII, ref. 1.

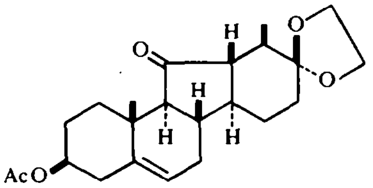
[†] The designations "etiojervane and jervane" will be used to describe 17aβ-methyl-C-nor-D-homo-18-nor-5α,13β-androstane and the corresponding cholestane analog, respectively.[7]

[‡] After we had completed this work, the synthesis of C-nor-D-homoprogesterone derivatives was reported by Kupchan and El-Haj (Ref. 4c). It is of interest that their synthesis has also been initiated by the introduction of a side chain to C_{17} of III.

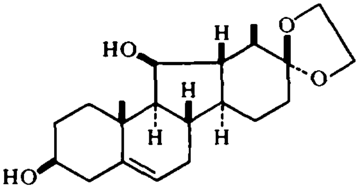
Before alkylation, it was necessary to establish the configuration at C_{12} of the ketone III. Kupchan and El-Haj[4c] assigned the β-configuration to the hydrogen of C_{12} on the basis of the NMR spectral studies. The same conclusion was drawn from the following facts. Treatment of 3-acetate[9a] (IIIa) of III with ethylene glycol in refluxing benzene containing *p*-toluenesulphonic acid (PTS) gave the corresponding 17-ethylene ketal (IV), m.p. 186–188°, which was then reduced with LAH to the 11β-alcohol (V), m.p. 167–168°. Deketalization of V with acid afforded 17-ketone (VI), m.p. 195–198°, in an over-all yield of 62% (3 steps), which on partial acetylation gave the 3-acetate (VIa), m.p. 134–136°. These 17-ketones VI and VIa exhibited negative Cotton effects with the amplitudes (dioxan) of −112° and −104°. These values were consistent with the stereostructure of C/D *trans*-fused linkage (12βH) and α-hydrogen configuration at C_{13} in the compounds, considering the amplitudes of B-norcholestan-3-one (+101°),[10] etiojerv-5-ene-3,17-dione 3-ethyleneketal (−92°)[4a] and B-norcoprostan-3-one (−69°).[10] The ketoacetate VIa was reconverted by oxidation with chromic anhydride in pyridine into the original ketone IIIa in 60% yield. This finding indicates that no epimerization at C_{12} is involved during the above-mentioned transformation and the C ring of III is, therefore, *trans*-fused with the D-ring (12βH). It is noteworthy that the ORD curve of the 11-ketone IV showed a negative Cotton effect with the amplitude of −172° and the ketone IIIa was recovered unchanged on treatment under the conditions of acid hydrolysis followed by re-acetylation.



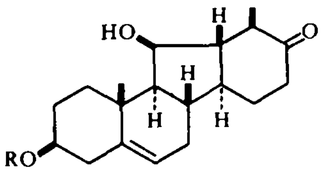
III: R = H
IIIa: R = Ac



IV



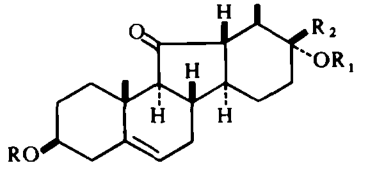
V



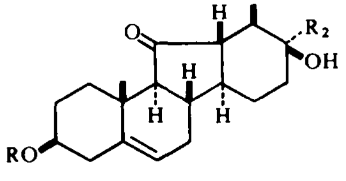
VI: R = H
VIa: R = Ac

Alkylation at C_{17} was attempted under various conditions to prepare compounds with 17-substituents convertible to the side chain of cortisone. The Wittig reaction of III with carbethoxymethylenetriphenylphosphorane[11,12] led to recovery of the starting material. Attempted cyanohydrin formation[13] gave unidentified compounds in low yields, most of III being recovered. Reactions with allylmagnesium bromide[14] afforded an intractable mixture; the IR spectra showed the absence of both 17- and 11-ketonic groups. Ethynylation with potassium or sodium acetylide in liquid ammonia[15] proved to be impractical, owing largely to the sensitivity of the C_{12}—C_{13} bond, flanked by two ketonic groups, to oxidation under the strongly alkaline conditions.

Successful alkylation was achieved by treatment of III with ethynylmagnesium bromide in THF at room temp,[16] whereby two ethynylcarbinols (VII), m.p. 222–224°, and (VIII), m.p. 159–162°, were obtained in 40% and 5% yields after chromatographic purification. Both the compounds VII and VIII were recovered unchanged after treatment with alkali in refluxing methanol for 22 hr, and were converted, by hydrogenation over platinum in ethanol, into the corresponding 17-ethylcarbinols (IX), m.p. 225–227°, and (X), m.p. 203–204°. The retention of configurations at C_{12} and C_{13} during the ethynylation was confirmed by ORD studies. The ORD curves of 3-monoacetates (VIIa to Xa), having m.ps 158–159°, 212–213°, 168–169° and 187–188°, of VII to X exhibited negative Cotton effects with practically the same amplitudes (−155°, −172°, −151° and −171°, respectively) as that of IV (−172°), indicative of the C/D *trans*-fusion and the 13α-hydrogen configuration. Furthermore, in view of the predominant axial attack by Grignard reagents on unhindered ketones,[17] the OH group at C_{17} was presumed to be α-oriented (equatorial) in the major product VII and β-oriented in the minor VIII. This assignment proved to be correct from the following bases. (i) Acetylation of VII with acetic anhydride and pyridine on a water-bath for 2 hr afforded the 3,17-diacetate (VIIb), m.p. 220–223°, in 72% yield along with the 3-monoacetate VIIa, while the same treatment of VIII effected only acetylation of the 3-OH group to give VIIIa in 80% yield. (ii) Compound VII was more strongly adsorbed on acid-washed alumina than VIII.[18] These facts indicate that the 17-OH group of VII is oriented equatorial and must be assigned α-configuration. Thus compound VII possesses the same configuration at C_{12}, C_{13} and C_{17} as cortisone.



VII: $R = R_1 = H;\ R_2 = C{\equiv}CH$
VIIa: $R = Ac;\ R_1 = H;\ R_2 = C{\equiv}CH$
VIIb: $R = R_1 = Ac;\ R_2 = C{\equiv}CH$
IX: $R = R_1 = H;\ R_2 = CH_2CH_3$
IXa: $R = Ac;\ R_1 = H;\ R_2 = CH_2CH_3$
XI: $R = R_1 = H;\ R_2 = CH{=}CH_2$
XIa: $R = Ac;\ R_1 = H;\ R = CH{=}CH_2$



VIII: $R = H;\ R_2 = C{\equiv}CH$
VIIIa: $R = Ac;\ R_2 = C{\equiv}CH$

X: $R = H;\ R_2 = CH_2CH_3$
Xa: $R = Ac;\ R_2 = CH_2CH_3$
XII: $R = H;\ R_2 = CH{=}CH_2$
XIIa: $R = Ac;\ R_2 = CH{=}CH_2$

Attempted hydration [19, 20] of the 17-ethynyl group in VII or transformation of the group in VIIb to a dibromoacetyl group (NBA, NaOAc–AcOH, 2 hr, 20°)[21] was unsuccessful; under mild conditions the starting materials were recovered and under vigorous conditions only intractable mixtures were obtained. The successful approach for conversion of the ethynyl group to the cortisone side chain started with reduction of the group. Treatment of VII with hydrogen in the presence of Lindlar catalyst[22] in ethyl acetate effected partial hydrogenation of the triple bond to give 17-vinylcarbinol (XI), m.p. 176–177°, in 90% yield. Compound VIII was likewise transformed to the vinylcarbinol (XII), m.p. 191–192°, in 75% yield. These compounds XI and XII showed negative Cotton effects with amplitudes of −153° and −173°, indicative of retention of the configuration at C_{12}, and gave on acetylation the respective 3-acetates (XIa), m.p. 135–136°, and (XIIa), m.p. 162–163°. In accordance with the assigned structures, the NMR spectra of XIa and XIIa exhibited, in the low fields, quartets due to the 20-protons with coupling constants of (10 and 17·5 c/s) and (10 and 18 c/s) at τ 3·88 and 4·17 besides signals due to the 6- and 21-protons. Further Oppenauer oxidation of XI afforded an α,β-unsaturated ketone (XIII), m.p. 183–184°, in 83% yield, which showed absorption maxima assignable to an α,β-unsaturated ketonic grouping at 235 mμ (ε 14,900) and at 1653 and 1616 cm^{-1} in the UV and IR spectra, respectively. The fact that the 3-acetate XIa was reconverted by saponification into the original alcohol XI in an almost quantitative yield indicated that the 12-configuration in XI was unaffected under alkaline conditions and, accordingly, would not epimerize during the Oppenauer oxidation. This was also supported by comparison of the ORD curve of XIII ($a = -155°$) with that of XI (−153°) and XII (−173°).*

Several attempts for conversion of 17-vinylcarbinol XIII to a hydroxypropylidene derivative were made with the expectation of that, if the allyl rearrangement proceeded successfully, the product could be transformed into C-nor-D-homocortisone by one-step oxidation according to the procedure of Miescher and Schmidlin.[23] Treatment of XIII with acetic anhydride in trichloroacetic acid[24] or with phosphorus tribromide[25] afforded intractable mixtures of the products. An attempted rearrangement of XIII under the ketalization at C_3 gave rise to a complex mixture; a major fraction separated in 40% yield by preparative TLC showed the presence of 3-ethyleneketal (singlet at τ 6·08) and an 11-oxo group (1730 cm^{-1}) in the spectra, but lacked a hydroxyl group (no absorption band near 3400 cm^{-1}), indicative of that it would be a mixture of $\Delta^{13(17)}$- and Δ^{16}-isomers (a doublet near τ 8·7 and a singlet at τ 7·84 due to the 18-Me group).

Next, selective oxidation of XIII was undertaken using the difference in nucleophilicity between the double bonds at C_4—C_5 and C_{17}—C_{20}. Epoxidation under mild conditions (−10°) led to only recovery of the starting material.† Compound XIII was then treated with osmium tetroxide in a mixture of THF and benzene at room temp for 2 days. While the starting material was recovered in 26% yield, the resulting osmate esters, after decomposition with sodium sulphite in refluxing aqueous ethanol,[27] gave a mixture of epimeric 20,21-glycols in 36% yield, which resisted further purification. The mixture was then acetylated with 1·3 equiv of acetic anhydride in a mixture of dioxan and pyridine at room temp for 16 hr.[15] The products (2 spots) were separated by preparative TLC to give a crystalline compound (XIV), m.p. 192–193°, and a semi-solid mixture in 26 and 56% yields, respectively.

Compound XIV was analysed for $C_{23}H_{32}O_6$, which corresponded to a molecular formula for glycol monoacetate of XIII. The IR and UV spectra showed the presence of an acetoxyl group at 1716 and 1235 cm^{-1} as well as a Δ^4-3-ketonic group at 236 mμ (ε 15,300) and at 1658 and 1621 cm^{-1}. In the NMR spectrum three quartets

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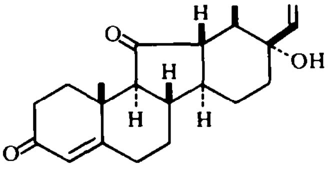
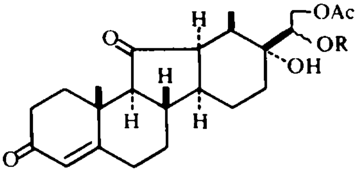
* Compare the ORD curves of compounds XI and XII in Ref. 4c with the respective Oppenauer oxidation products VII and VIII.

† Treatment of 17α-acetyletiojerv-4-en-3-one with perbenzoic acid in chloroform at room temp for 23 hr resulted in formation of 17α-acetoxy-3,4-oxido-ε-lactone as a main product.[26]

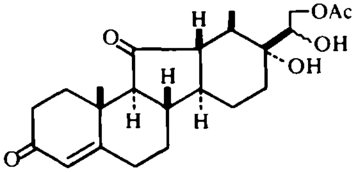
appeared at τ 5·61, 5·93 and 6·28, which were split with coupling constants of (11·5 and 2·5 c/s), (11·5 and 7·2 c/s) and (7·2 and 2·5 c/s), respectively, and attributable to three protons on the C atoms bearing the OAc (C_{21}) and OH groups (C_{20}). These spectral behaviour is consistent with the assigned structure for XIV and also confirms that XIV is not 20-acetate but 21-acetate. On the other hand, recrystallization of the semi-solid material resulted in isolation of glycol diacetate (XIVa) $C_{25}H_{34}O_7$, m.p. 218–219°, in 50% yield (of the material). This compound shows a NMR spectrum closely related to that of XIV; absorptions assignable to protons on C_{20} and C_{21} bearing OAc groups were observed at τ 4·85, 5·45 and 5·92 as clear quartets with coupling constants of (8·5 and 2·5 c/s), (11·0 and 2·5 c/s) and (11·0 and 8·5 c/s). This suggests that XIVa is a 20-O-acetyl derivative of XIV, which was confirmed by saponification of XIVa followed by partial acetylation to XIV. The mother liquor obtained on the recrystallization gave amorphous substance (XV), which proved to be a mixture of XIVa and a 12- [and also 20- (?)] epimer (XIV′) of XIV by oxidation experiments described later.



XIII



XIV: R = H
XIVa: R = Ac



XIV′

The ORD curve of XIV shows a negative Cotton effect, but the amplitude, to the contrary of the expectation, decreased markedly to −91° as compared with that (−155°) of XIII. This decrease is readily explicable in terms of octant rule considerations for cyclopentanone derivatives, which have been advanced by Klyne[28] and have recently been applied effectively for 11-oxojervanes and 11-oxoetiojervanes,[29]* and suggests the C/D *cis*-junction in XIV. The formation of this C/D *cis*-fused compound XIV can be rationalized by assuming that XIII having the C/D *trans*-juncture underwent epimerization at C_{12} during the decomposition of the bulky osmate esters on the axial 17-side chain under the alkaline conditions. In fact, prolonged treatment of the esters with sodium bisulphite followed by monoacetylation produced XIV as a major product. This configurational assignment to XIV will be confirmed by oxidation experiments described later.

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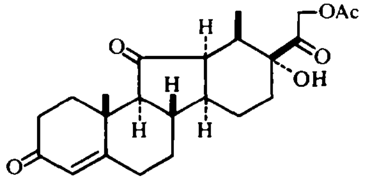
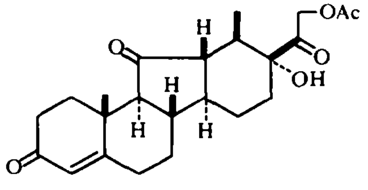
* Compare the ORD curves of compounds V and VI in Ref. 4c.

Oxidation of XIV with Jones reagent[30] produced a mixture showing three spots, which was purified by preparative TLC to give the starting material XIV, 17β-acetoxyacetyl-12α-etiojerv-4-ene-3,11-dion-17α-ol (XVI), m.p. 191–193°, and a triketone (XVII), m.p. 171–174°, in yields of 40, 20 and 15%. Compound XVI, $C_{23}H_{30}O_6$, exhibited the spectra consistent with the assigned structure; e.g. in the NMR spectrum a doublet ($J = 7{\cdot}7$ c/s) due to 18-Me protons and two singlets due to 19-Me protons and an OAc group appeared at τ 9·17, 8·76 and 7·84 in the higher field, and a quartet of AB type ($J = 16$ c/s) due to two protons at C_{21} and a singlet due to that at C_4 were observed at τ 4·98 and 4·26, respectively, in the lower field. On the other hand, the elementary analysis of XVII fitted a molecular formula $C_{19}H_{24}O_3$ corresponding to that of a known cleavage product, etiojerv-4-ene-3,11,17-trione[4a] (XVIII). The UV spectrum of XVII shows the presence of a Δ^4-3-ketonic group at 234 mμ (ε 18,300). The IR spectrum also indicates absorption maxima attributed to this functional group as well as 5-membered and 6-membered ring ketonic groupings at 1670, 1623, 1732 and 1714 cm^{-1}, and was superimposable over that of XVIII as far as the absorption near 1700 cm^{-1} concerned. However, the spectrum differs definitely from that of XVIII in the finger-print region, indicating that compound XVII is a 12α-epimer of XVIII.

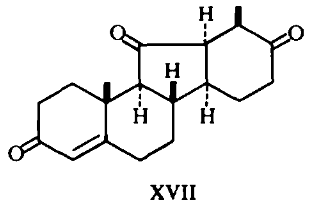
Similarly, the amorphous substance XV, described in the previous section, was oxidized with Jones reagent without further purification. The product consisted of three compounds, which were separated by repeated preparative TLC. The least mobile compound, isolated in 43% yield, proved to be diacetate XIVa, implying that XIVa was originally included in XV and recovered unchanged from the reaction product. Of the remaining two compounds, the more polar, m.p. 212–214°, was isolated in 8% yield and identified as the known compound, triketone XVIII. The less polar compound, m.p. 203–204°, isolated in 32% yield, had a molecular formula of $C_{23}H_{30}O_6$ and proved to be an aimed compound, 17β-acetoxyacetyletiojerv-4-ene-3,11-dion-17α-ol (XIX) on the basis of the spectral data; namely, in accordance with the assigned structure, XIX shows an absorption maximum at 234 mμ (ε 16,800) due to a Δ^4-3-ketonic group. In the IR spectrum absorption maxima assignable to hydroxyl, 11-ketonic, acetoxyl, 20-ketonic and Δ^4-3-ketonic groups are observed at



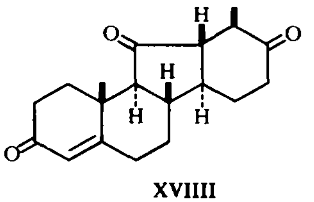
XVI



XIX



XVII



XVIIII

3354, 1740, 1740 (and 1256), 1722 and 1650 (and 1615) cm^{-1}. The NMR spectrum exhibits 3-proton signals at τ 8·81 (singlet), 8·72 (doublet, $J = 6·2$ c/s) and 7·84 (singlet), a two-proton quartet of AB type ($J = 17$ c/s) at τ 5·05, and a one-proton singlet at τ 4·26, which were attributed to 19-Me, 18-Me, OAc, 21-methylene and 4-olefinic protons, respectively. Judging from the total yield (83%), the oxidation result suggested that XV consists mainly of XIVa and 20,21-glycol 21-monoacetate with C/D *trans*-fused linkage (XIV′), a 12- [and also 20- (?)] epimer of XIV, as described already. This was supported by examination of the NMR spectrum; XV exhibited, in the higher field, only two singlets at τ 8·80 and 8·74, the former having practically the same chemical shift as the 19-Me protons (τ 8·81) of XIX and the latter as those (τ 8·73) of XIVa. Thus the latter peak must be assigned to the Me protons of XIVa and the former to those of XIV′, because the deshielding effect of substituents at C_{20} to 19-Me protons would be negligibly small.

Now it has been established that both XIX and XVI are formulated as 17β-acetoxyacetyletiojerv-4-en-17α-ol-3,11-dione and have the same configurations at all the asymmetric centres except the 12-C atom. Since compound XIX has been isolated along with the 12β-triketone XVIII and XVI has been derived from 12α-glycol XIV and accompanied by 12α-triketone XVII, the configuration of C_{12} may be reasonably assigned β (C/D *trans*) in XIX and α (C/D *cis*) in XVI. This configurational assignment is supported by the NMR spectra; the 19-Me protons (τ 8·81) of XIX appeared at a slightly but definitely higher field than that (τ 8·76) of XVI.[1] Compound XIX may, therefore, be regarded as C-nor-D-homocortisone 21-acetate, since it possesses the cortisone configuration at each of the ring junctions and XVI at its 13α-epimer.

EXPERIMENTAL

All the m.ps are uncorrected. The homogenity of each compound was always checked by TLC on silica gel (Wakogel B-5) using various solvent systems, and the spots were developed with cerric sulphate in dil H_2SO_4 and/or I_2. The optical rotations, ORD curves, UV and IR spectra were measured in MeOH, dioxan, 95% EtOH and Nujol, respectively, unless otherwise stated. The NMR spectra were obtained in $CDCl_3$ at 60 Mc, and the chemical shifts were given in τ-values, using TMS as an internal reference. The abbreviations "s, d, q and m" in the NMR spectra denote "singlet, doublet, quartet and multiplet," respectively.

O-*Acetyletiojerv-5-en-3β-ol-11,17-dione 17-ethyleneketal* (IV)

Compound IIIa[9] (800 mg), m.p. 168–170°, was dissolved in a mixture of benzene (80 ml) and ethylene glycol (3 ml) containing PTS (42 mg as hydrate), and the soln was refluxed for 19 hr under stirring, water being removed under a Dean–Stark apparatus. After being cooled the mixture was washed with 5% $NaHCO_3$aq and water, dried and evaporated to dryness. The residue (953 mg) was crystallized from a mixture of isopropyl ether (10 ml) and n-hexane (15 ml) to give IV (841 mg), m.p. 181–182°. Recrystallization from isopropyl ether gave an analytical sample, m.p. 186–188°; $[\alpha]_D^{22}$ −134° ($CHCl_3$); IR, ν_{max} 1730, 1241 and 1084 cm^{-1}; NMR, τ 8·95 (3H, s, 19-Me), 8·81 (3H, d $J = 5·3$ c/s, 18-Me), 7·98 (3H, s, OAc), 6·04 (4H, s, —OCH_2CH_2—) and 5·43 (1H, m, 3-H) and 4·63 (1H, d $J = 4·5$ c/s, 6-H); ORD, $[\phi]_{332}^{trough}$ −10,900°, $[\phi]_{291}^{peak}$ +6260°, $a = -172°$. (Found: C, 70·95; H, 8·38. $C_{23}H_{32}O_5$ requires: C, 71·10; H, 8·30%).

Etiojerv-5-ene-3β,11β-diol-17-one 17-ethyleneketal (V)

A soln of IV (700 mg) in dry ether (100 ml) containing LAH (716 mg) was refluxed under stirring for 14 hr and cooled with ice-water. To the soln was cautiously added water and 1N H_2SO_4 (40 ml) to decompose excess of the LAH and the complex formed, and the aqueous soln was extracted repeatedly with ether. All the ether extracts were combined, washed with 5% $NaHCO_3$aq and water, dried and evaporated. The residue (762 mg) crystallized on trituration with ether to yield V (494 mg), m.p. 165–166°. Recrystallization from ether gave an analytical sample, m.p. 167–168°; $[\alpha]_D^{22}$ −38° ($CHCl_3$); IR, ν_{max} 3470, 3310, 1117, 1085 and

1051 cm^{-1}; NMR τ 8·97 (3H, d J = 6·0 c/s, 18-Me), 8·73 (3H, s, 19-Me), 6·57 (1H, m, 3-H), 6·03 (4H, s, —OCH$_2$CH$_2$O—), 5·87 (1H, m, 11-H), and 4·75 (1H, d J = 3·5 c/s, 6-H). (Found: C, 72·22; H, 9·23. $C_{21}H_{32}O_4$ requires: C, 72·38; H, 9·26%).

Etiojerv-5-ene-3β,11β-diol-17-one (VI)

Compound V (364 mg) was dissolved in a soln of acetone (60 ml) and water (6 ml) containing PTS (40 mg) and refluxed for 3 hr. After removal of the solvents below 23° under reduced press, the residue was extracted with CHCl$_3$, and the CHCl$_3$ soln was washed with 5% NaHCO$_3$aq and water, dried and evaporated to give an amorphous residue (367 mg). Trituration with acetone afforded VI (266 mg), m.p. 193–195°, which was recrystallized from the same solvent to give an analytical sample. m.p. 195–198°; $[\alpha]_D^{22}$ −85·8°; IR, ν_{max} 3415, 1690 and 1053 cn^{-1}; NMR, 8·85 (3H, d J = 6·3 c/s, 18-Me), 8·73 (3H, s, 19-Me), 6·47 (1H, m, 3-H), 5·69 (1H, m, 11-H), and 4·73 (1H, d J = 6 c/s, 6-H); ORD, $[\phi]_{318}^{trough}$ −8020°, $[\phi]_{276}^{peak}$ +3180°, a = −112°. (Found: C, 75·05; H, 9·35. $C_{19}H_{28}O_3$ requires: C, 74·96; H, 9·27%).

Compound VI (155 mg) was treated with Ac$_2$O (1·5 ml) and pyridine (2 ml) at room temp for 3 hr. The soln was poured into ice–water, and the white ppt (164 mg) was collected, dried, and crystallized from isopropyl ether to give the acetate VIa (140 mg), m.p. 132–134°. Two recrystallizations from isopropyl ether gave an analytical sample, m.p. 134–136°; $[\alpha]_D^{22}$ −84·1° (CHCl$_3$); IR, ν_{max} 3485, 1724, 1705, 1244 and 1030 cm^{-1}; NMR, τ 8·85 (3H, d J = 6 c/s, 18-Me), 8·72 (3H, s, 19-Me), 7·95 (3H, s, OAc), 5·63 (1H, m, 11-H), 5·34 (1H, m, 3-H), and 4·70 (1H, d J = 3·8 c/s, 6-H); ORD, $[\phi]_{308}^{trough}$ −6510°, $[\phi]_{276}^{peak}$ +3850°, a = −104°. (Found: C, 71·08; H, 8·68. $C_{21}H_{30}O_4 \cdot \frac{1}{2}H_2O$ requires: C, 70·99, H, 8·73%).

The acetate VIa (42 mg) was dissolved in pyridine (1 ml), and cooled at 0°. To the soln was added CrO$_3$ (104 mg), and the mixture was stirred at room temp for 25 hr. After addition of water, the whole mixture was shaken with 1N HCl, 5% NaHCO$_3$aq and saturated NaClaq, dried and evaporated to yield crystalline residue (44 mg), showing only one spot with the same R_f value as IIIa. Recrystallization from isopropyl ether gave IIIa (25 mg), m.p. 170–171°, which showed the IR spectrum identical with that of an authentic sample of IIIa.

17β-Ethynyletiojerv-5-ene-3β,17α-diol-11-one (VII) *and the 17-epimer* (VIII)

In a 3-necked flask fitted with a condenser, a separating funnel and a glass tube for introduction of gas was placed dry, freshly distilled THF (150 ml), and acetylene gas was passed to the THF at room temp for 10 min. To the soln was added dropwise EtMgBr, prepared from Mg metal (6·5 g) and EtBr (21 ml) in THF (150 ml), during 10 min, when acetylene was bubbled continuously. Acetylene gas was further passed for 1·5 hr and compound III (2·29 g) in dry THF (30 ml) was added to the soln during 15 min. The whole mixture was then allowed to stand under stirring at room temp for 24 hr. To the mixture cooled with ice-water was added saturated NH$_4$Claq (33 ml), and the ppt collected by filtration and washed with CHCl$_3$. The aqueous THF soln was evaporated under reduced press to remove THF and extracted with CHCl$_3$ repeatedly. All the CHCl$_3$ washings and extracts were combined, washed with 5% NaHCO$_3$aq, dried with Na$_2$SO$_4$, and evaporated to dryness to yield tarry residue (2·9 g). Similarly, from 6·79 g of III there was obtained 8·6 g of the same tarry residue.

The residues obtained in the two runs were combined and chromatographed over acid-washed Al$_2$O$_3$ (Woelm I, 230 g) using the following solvents successively; benzene–ether (3:1); (1:1); (1:2); (1:3); (1:4); ether. Fractions eluted with benzene–ether (3:1) crystallized on removal of the solvents and recrystallization from a mixture of acetone and benzene gave a pure sample of VIII (168 mg), m.p. 159–162°; $[\alpha]_D^{19}$ −153·4°; IR, ν_{max} 3278, 1720 and 1040 cm^{-1}. (Found: C, 75·28; H, 8·56. $C_{21}H_{28}O_3 \cdot \frac{1}{2}C_3H_6O$ requires: C, 75·63; H, 8·68%). Fractions with benzene–ether (1:1 to 1:4) and ether were crystallized on removal of the solvents and recrystallization from acetone–benzene afforded a pure sample of VII (2·41 g), m.p. 222–224°; $[\alpha]_D^{19}$ −115·7°; IR, ν_{max}, 3425, 3278, 1728 and 1041 cm^{-1}. (Found: C, 75·31; H, 8·67. $C_{21}H_{28}O_3 \cdot \frac{1}{2}C_3H_6O$ requires: C, 75·63; H, 8·68%). The mother liquors were combined, evaporated and purified by preparative TLC to yield VII (528 mg), m.p. 219–222°, and VIII (340 mg), m.p. 154–160°.

Compound VII (100 mg) was acetylated with Ac$_2$O (1·5 ml) and pyridine (2 ml) at room temp for 2 hr. The mixture afforded the 3-monoacetate (VIIa) in a quantitative yield, m.p. 158–159° (from acetone–isopropyl ether); $[\alpha]_D^{18}$ −83·0°; IR, ν_{max} 3420, 3260, 1732, 1712, 1263, and 1029 cm^{-1}; NMR, τ 8·88 (3H, s, 19-Me), 8·56 (3H, d J = 4·8 c/s, 18-Me); 7·90 (3H, s, OAc), 7·47 (1H, s, 21-H), 5·38 (1H, m, 3-H), and 4·52 (1H, d J = 4·5 c/s); ORD, $[\phi]_{333}^{trough}$ −9710°, $[\phi]_{292}^{peak}$ +5780°, a = −155°. (Found: C, 74·65; H, 8·33. $C_{23}H_{30}O_4$ requires: C, 74·56; H, 8·16%).

Compound VII (100 mg) was treated with Ac$_2$O (1 ml) and pyridine (2·5 ml) on a water-bath for 2 hr.

After removal of the solvents the residue was separated by preparative TLC to yield VIIa (39 mg), m.p. 158–159° (from acetone–isopropyl ether), and 3,17-diacetate VIIb (82 mg), m.p. 220–223° (from acetone); $[\alpha]_D^{18}$ $-63{\cdot}2°$ ($CHCl_3$); IR, ν_{max} 3218, 1732, 1722, and 1238 cm^{-1}; NMR, τ 8·88 (3H, s, 19-Me), 8·55 (3H, d J = 5·7 c/s, 18-Me), 7·85 (6H, s, OAc), and 7·30 (1H, s, 21-H). (Found: C, 72·55; H, 7·74. $C_{25}H_{32}O_5$ requires: C, 72·79; H, 7·82%).

Compound VIII (104 mg) was acetylated with Ac_2O (1·5 ml) and pyridine (2 ml) at room temp for 12 hr. The mixture afforded the monoacetate VIIIa (73 mg), m.p. 212–213° (from acetone–isopropyl ether); $[\alpha]_D^{18}$ $-117{\cdot}4°$; IR, ν_{max} 3460, 3225, 1723, 1250, and 1040 cm^{-1}; NMR, τ 8·93 (3H, s, 19-Me), 8·54 (3H, d J = 4·8 c/s, 18-Me); 7·94 (3H, s, OAc), and 7·50 (1H, s, 21-H); ORD, $[\phi]_{332}^{trough}$ $-11510°$, $[\phi]_{292}^{peak}$ $+5730°$, $a = -172°$. (Found: C, 74·69; H, 8·10. $C_{23}H_{30}O_4$ requires: C, 74·56; H, 8·16%).

Compound VIII (70 mg) was treated with Ac_2O (1 ml) and pyridine (2 ml) on a water-bath for 4 hr. After removal of the solvents the residue was purified by preparative TLC to yield VIIIa (59 mg), m.p. 213–214° (from acetone–isopropyl ether) and an unidentified material (15 mg), amorphous.

17β-*Ethyletiojerv-5-ene*-3β,17α-*diol*-11-*one* (IX)

Compound VII (196 mg) was hydrogenated in the presence of pre-reduced Pt (121 mg as Adams PtO_2) at room temp in 99% EtOH (20 ml) and the reaction was ceased after 2 hr, when 48 ml of H_2 (1·1 mol) had been absorbed. After removal of the catalyst and the solvent, the residue was crystallized from acetone and collected by filtration to yield IX (118 mg). Recrystallization from acetone gave a pure sample of IX, m.p. 225–227°, $[\alpha]_D^{17}$ $-137{\cdot}4°$; IR, ν_{max} 3350, 1728, 1043 and 970 cm^{-1}. (Found: C, 75·69; H, 9·68. $C_{21}H_{32}O_3$ requires: C, 75·86; H, 9·70%).

Compound IX (75 mg) was acetylated with Ac_2O (1 ml) and pyridine (1 ml) at room temp for 5 hr. The mixture was worked up as usual and the residue was crystallized from acetone–isopropyl ether. Recrystallization from the same solvent afforded the 3-acetate (IXa, 68 mg), m.p. 168·5–169°; $[\alpha]_D^{17}$ $-126{\cdot}1°$; IR, ν_{max} 3460, 1726, 1265, 1239, 1139, 1038, and 972 cm^{-1}; NMR, τ 8·94 (3H, s, 19-Me), 8·77 (3H, d J = 5·4 c/s, 18-Me), 7·98 (3H, s, OAc); ORD, $[\phi]_{333}^{trough}$ $-11{,}000°$, $[\phi]_{291}^{peak}$ $+4100°$, $a = -151°$. (Found: C, 73·72; H, 9·12. $C_{23}H_{34}O_4$ requires: C, 73·76; H, 9·15%).

17α-*Ethyletiojerv-5-ene*-3β,17β-*diol*-11-*one* (X)

Compound VIII (117 mg) was hydrogenated over pre-reduced Adams' Pt (73 mg) at room temp in EtOH (10 ml) and the reaction was ceased after 2 hr, when 28 ml of H_2 (1·1 mol) had been consumed. The mixture was worked up in the same way as that of VII and gave X (98 mg), m.p. 203–204°, on recrystallization from acetone; $[\alpha]_D^{17}$ $-136{\cdot}2°$; IR, ν_{max} 3490, 3420, 1712, 1051, and 948 cm^{-1}. (Found: C, 75·81; H, 9·67. $C_{21}H_{32}O_3$ requires: C, 75·86; H, 9·70%).

Acetylation of X (60 mg) with Ac_2O (1 ml) and pyridine (1 ml) at room temp for 3 hr afforded the 3-acetate (Xa, 45 mg), m.p. 187–188° (from acetone); $[\alpha]_D^{17}$ $-117{\cdot}7°$; IR, ν_{max} 3510, 1718, 1262, and 1041 cm^{-1}; NMR; 8·93 (3H, s, 19-Me), 8·78 (3H, d J = 5·5 c/s, 18-Me), 8·00 (3H, s, OAc) and 4·17 (1H, q, J = 1·5 and 4·5 c/s); ORD, $[\phi]_{333}^{trough}$ $-10{,}910°$, $[\phi]_{292}^{peak}$ $+6170°$, $a = -171°$. (Found: C, 73·76; H, 9·15. $C_{23}H_{34}O_4$ requires: C, 73·75; H, 9·18%).

17β-*Vinyletiojerv-5-ene*-3β,17α-*diol*-11-*one* (XI)

17β-Ethynylcarbinol VII (490 mg) was hydrogenated in the presence of Lindlar catalyst[23] (800 mg), shaken with H_2 in advance, at room temp in EtOAc (75 ml). The reaction was ceased after 1·5 hr, when 36 ml of H_2 (1·0 mol) had been consumed. After the removal of the catalyst and the solvent, the residue crystallized on trituration with acetone and was recrystallized from acetone–isopropyl ether to give XI (442 mg), m.p. 176–177°; $[\alpha]_D^{19}$ $-147{\cdot}6°$; IR, ν_{max} 3310, 1728, 1653, 1040, 995, and 922 cm^{-1}; ORD, $[\phi]_{334}^{trough}$ $-9940°$, $[\phi]_{292}^{peak}$ $+5320°$, $a = -153°$. (Found: C, 73·29; H, 9·18. $C_{21}H_{30}O_3\cdot\frac{3}{2}C_3H_6O$ requires: C, 73·38; H, 9·35%).

Acetylation of XI (58 mg) with Ac_2O (0·7 ml) and pyridine (1 ml) at room temp for 3 hr afforded the 3-acetate (XIa, 38 mg), m.p. 135–136°, after recrystallization from isopropyl ether; $[\alpha]_D^{17}$ $-130{\cdot}7°$; IR, ($CHCl_3$), ν_{max} 1729, 1250, 1035, and 995 cm^{-1}; NMR, τ 8·94 (3H, s, 19-Me), 8·78 (3H, d J = 6·2 c/s, 18-Me), 7·97 (3H, s, OAc), and 3·88 (1H, q J = 10 and 17·5 c/s, 20-H). (Found: C, 74·13; H, 8·70. $C_{23}H_{32}O_4$ requires: C, 74·16; H, 8·66%).

17α-*Vinyletiojerv-5-ene*-3β,17β-*diol*-11-*one* (XII)

17α-Ethynylcarbinol VIII (180 mg) was hydrogenated over Lindlar catalyst (450 + 427 mg) at room temp in EtOH and the reaction was continued, until ca. 1 mol of H_2 (15 ml) was absorbed (about 2·5 hr). The product was worked up as usual and gave XII (135 mg), m.p. 191–192°, after recrystallization from acetone–isopropyl ether: $[\alpha]_D^{18}$ −96·1°: IR, ν_{max} 3410, 1722, 1645, 1047, 965, and 916 cm^{-1}; ORD, $[\phi]_{333}^{trough}$ −11,100°, $[\phi]_{292}^{peak}$ +6220°, $a = -173$. (Found: C, 76·17; H, 9·38. $C_{21}H_{30}O_3$ requires: C, 76·32; H, 9·15%).

Acetylation of XII (71 mg) with Ac_2O (1 ml) and pyridine (1 ml) at room temp for 12 hr gave the 3-acetate (XIIa, 43 mg), m.p. 162–163° (from isopropyl ether); $[\alpha]_D^{17}$ −16·6°; IR ν_{max} 3486, 1719, 1249, 1044, 973, and 924 cm^{-1}; NMR, τ 8·93 (3H, s, 19-Me), 8·83 (3H, d J = 6 c/s, 18-Me), 7·95 (3H, s, OAc), and 4·17 (1H, q J = 10 and 18 c/s). (Found: C, 74·34; H, 8·66. $C_{23}H_{34}O_4$ requires: C, 74·16; H, 8·66%).

17β-*Vinyletiojerv-4-en-*17α-*ol*-3,11-*dione* (XIII)

A soln of XI (358 mg) in toluene (150 ml, redistilled) containing cyclohexanone (3·4 ml, redistilled) was heated under stirring to distil about 80 ml of toluene to dry the system. To the stirred, refluxing soln was added aluminum isopropoxide (402 mg), and the whole mixture was refluxed for 70 min and then cooled. The mixture was distilled with steam until most of the solvents had been removed, and the residue was, after being cooled, extracted with $CHCl_3$ repeatedly. The $CHCl_3$ soln was washed in HCl, 5% $NaHCO_3$aq and water, dried and evaporated to dryness. The residue was crystallized from acetone and recrystallized from acetone–isopropyl ether to give XIII (299 mg), m.p. 183–184°; $[\alpha]_D^{18}$ −37·7°; UV, λ_{max} 235 mμ (ε 14,900); IR, ν_{max} 3370, 1730, 1653, 1616, 1136, 995, 930, and 870 cm^{-1}; ORD, $[\phi]_{334}^{trough}$ −9820°, $[\phi]_{292}^{peak}$ +5670°, $a = -155°$. (Found: C, 76·75; H, 8·49. $C_{21}H_{28}O_3$ requires: C, 76·79; H, 8·59%).

Hydroxylation of XIII *with osmium tetroxide*

17β-*Ethyletiojerv-4-ene-*17α,20,21-*triol*-3,11-*dione* 21-*acetate* (XIV). To a soln of XIII (1·027 g) in THF (15 ml) and benzene (5 ml) was added OsO_4 (944 mg), and the whole soln was allowed to stand at room temp. After 2 days the osmate ppt was collected by filtration and amounted to 1·79 g. The osmate was dissolved in EtOH (200 ml) and then mixed with Na_2SO_3 (8 g) in water (45 ml). The suspended mixture was refluxed on a water-bath for 3 hr, cooled and filtered. The ppt was washed with hot EtOH, and the EtOH washings were combined with the filtrate. The combined soln was evaporated to remove EtOH and shaken with $CHCl_3$ repeatedly. The $CHCl_3$ extracts were washed with 1N HCl and water, dried with Na_2SO_4 and evaporated to dryness, yielding amorphous residue (401 mg). The ppt which remained undissolved on being washed with hot EtOH was treated in the same manner (EtOH 150 ml, Na_2SO_3 8 g and water 45 ml, refluxing for 3·5 hr) as the osmate ppt and yielded amorphous residue (20 mg). On the other hand, the filtrate obtained on filtration of the first osmate was evaporated to dryness and the residue (0·37 g) treated in the same way (EtOH 58 ml, Na_2SO_3 2·5 g and water 15 ml, refluxing for 2 hr) as the osmate ppt to give crystalline substance (0·26 g), which was found to consist mainly of the starting material XIII by examination of the IR spectrum and TLC.

The amorphous substance (total 420 mg) was combined and a part (318 mg) was partially acetylated, without further purification, with Ac_2O (116 mg) and pyridine (0·75 ml) in dioxan (1·5 ml) at room temp for 17 hr. The soln was poured into ice-water and extracted with $CHCl_3$. The $CHCl_3$ soln was washed with 1N HCl, 5% $NaHCO_3$aq and water, dried and evaporated to dryness, yielding amorphous residue, which showed only two spots on TLC and was separated by preparative TLC. The less polar band was extracted with acetone, crystallized on removal of the solvent and amounted to 106 mg. Recrystallization from acetone gave 21-monoacetate XIV (87 mg), m.p. 192–193°; $[\alpha]_D^{16}$ +115·6° ($CHCl_3$); UV, λ_{max} 236 mμ (ε 15,300); IR, ν_{max} 3480, 3360, 1740, 1716, 1658, 1621, and 1235 cm^{-1}; NMR, τ 8·74 (3H, s, 19-Me), 9·08 (3H, d J = 7 c/s, 18-Me), 7·88 (3H, s, OAc), 6·28 (1H, q J = 2·5 and 7·2 c/s, 20-H), 5·93 (1H, q J = 11·5 and 7·2 c/s, 21-H), 5·61 (1H, q J = 2·5 and 11·5 c/s, 21-H), and 4·22 (1H, s, 4-H); ORD, $[\phi]_{334}^{trough}$ −2470°, $[\phi]_{292}^{shoulder}$ +6640°, $a = -91°$. (Found: C, 67·95; H, 7·82. $C_{23}H_{32}O_6$ requires: C, 68·29; H, 7·97%).

The more polar substance (179 mg), semi-solid, was treated with a small volume of acetone, when crystals separated out and were collected by filtration. Recrystallization from acetone afforded 20,21-diacetate (XIVa, 86 mg), m.p. 218–219°; $[\alpha]_D^{16}$ +85·5° ($CHCl_3$); UV, λ_{max} 236 mμ (ε 16,200); IR, ν_{max} 3430, 1737, 1723, 1658, 1613, 1225 and 1048 cm^{-1}; NMR, τ 8·73 (3H, s, 19-Me); 8·97 (3H, d J = 7·2 c/s, 18-Me); 7·98 and 7·85 (each 3H, s, OAc), 5·92, 5·45 and 4·85 (each 1H, each q J = 11·0 and 8·5, 11·0 and 2·5, and 8·5 and 2·5 c/s, 21-H and 20-H, respectively), and 4·23 (1H, s, 4-H). (Found: C, 67·06; H, 7·65. $C_{25}H_{34}O_7$ requires: C, 67·24; H, 7·58%). The filtrate obtained on filtration of the crystalline substance XIVa was evaporated to dryness and yielded amorphous residue (XV, 85 mg), which proved to be a mixture of XIVa, a glycol (XIV′) with *trans*-fused C/D linkage and convertible by oxidation into 20-ketone XIX, and triketone (XVIII); in the NMR spectrum two sharp singlets appeared at τ 8·80 and 8·74 assignable to 19-Me protons of XIV′ and XIVa, respectively, and the former showed higher intensity than the latter.

Compound XIVa (74 mg) was hydrolyzed with 5% KOH in refluxing MeOH (10 ml) for 50 min. After removal of the solvent, the residue was mixed with water and shaken with $CHCl_3$. The $CHCl_3$ soln was washed with 1N HCl and water, dried and evaporated to dryness. The residue (33 mg), which contained no XIVa (TLC), was acetylated with Ac_2O (10 mg) and pyridine (0·1 ml) in dioxan (0·2 ml) at room temp for 5 hr. The soln was poured into ice–water and then extracted with $CHCl_3$. The $CHCl_3$ soln was washed with 1N HCl, 5% $NaHCO_3$aq and water, dried and evaporated to dryness to yield amorphous residue, which was separated into two fractions by preparative TLC. Each fraction crystallized on trituration with acetone; one (10 mg), m.p. 216–218°, was identified as XIVa and the other (17 mg), m.p. 190–192°, as XIV, indicating that XIVa was a 20-O-acetyl derivative of XIV.

Oxidation of XIV *with Jones reagent*

17β-Acetoxyacetyl-12α-etiojerv-4-ene-3,11-dion-17α-ol (XVI) *and 12α-etiojerv-4-ene-3,11,17-trione* (XVII). To a soln of XIV (78 mg) in acetone (4 ml) was added Jones reagent (0·049 ml) under cooling with ice–water and stirring, and the mixture was further stirred at the temp. After 25 min the reaction was stopped by addition of EtOH, and the solvents were removed under reduced press. To the residue was added water, and the mixture was extracted with $CHCl_3$. The $CHCl_3$ soln was washed with 5% $NaHCO_3$aq and water, dried and evaporated to dryness to give an amorphous mixture (77 mg), which showed 3 spots and was separated by preparative TLC. The least polar band gave the starting material XIV (31 mg) after extraction with acetone and removal of the solvent. The middle band afforded a crystalline material (16 mg), which on recrystallization from EtOAc–isopropyl ether gave XVI, m.p. 191–193°; $[\alpha]_D^{22}$ +166° ($CHCl_3$); UV, λ_{max} 235 mμ (ε 18,800); IR, ν_{max} 3304, 1748, 1724, 1648, 1615, and 1232 cm^{-1}; NMR, τ 9·17 (3H, d J = 7·7 c/s, 18-Me), 8·76 (3H, s, 19-Me), 7·84 (3H, s, OAc), 5·16 and 4·80 (each 1H, q of AB type with J = 16 c/s, 21-H) and 4·26 (1H, s, 4-H); ORD, $[\phi]$ values +2310, +2050, +2310, +1410, +1540, +530°, +3630, +3340°, +3630°, +2650°, +2830°, + 2560° at 378, 370, 361, 351, 346, 337, 321, 316, 311, 304, 300, and 295 mμ. (Found: C, 69·28; H, 7·45. $C_{23}H_{30}O_6$ requires: C, 69·54; H, 7·30%).

The most polar band afforded a crystalline substance (12 mg), which on recrystallization from EtOAc–isopropyl ether gave XVII, m.p. 171–174°; UV, 234 mμ (ε 18,300); IR, ν_{max} 1732, 1714, 1670, and 1623 cm^{-1}. The IR spectrum (in Nujol) was remarkably different from that of XVIII. (Found: C, 76·04; H, 7·88. $C_{19}H_{24}O_3$ requires: C, 75·97; H, 8·05%).

Oxidation of the amorphous substance XV *with Jones reagent*

17β-Acetoxyacetyletiojerv-4-ene-3,11-dion-17α-ol (XIX) *and etiojerv-4-ene-3,11,17-triketone* (XVIII). A soln of the amorphous XV (64 mg) in acetone (5 ml) was treated with Jones reagent (0·040 ml) under cooling with ice–water and stirring. After 20 min the oxidation was ceased by addition of EtOH (1 ml), and the mixture was evaporated under reduced press to remove the solvents. The residue was mixed with water and extracted with $CHCl_3$. The $CHCl_3$ soln was washed with 5% $NaHCO_3$aq and water, dried, and evaporated to dryness to yield amorphous residue (56 mg), which was separated roughly into two fractions by preparative TLC (Wakogel B-5, ether). The less mobil fraction gave a crystalline substance (27 mg), which on recrystallization from EtOAc–isopropyl ether yielded diacetate XIVa, m.p. 215–217°. This sample was originally included in the starting substance XV and recovered unchanged after the oxidation.

The more mobile substance (29 mg) was again submitted to preparative TLC (Wakogel B-5, ether–benzene 3:2) and separated into two fractions. The more polar fraction gave a crystalline compound (5 mg), which on washing with acetone had m.p. 212–214 and proved to be the known cleavage product XVIII by comparison of the IR spectrum and TLC with those of an authentic sample. The less polar band was extracted with acetone and afforded a crystalline substance (20 mg) on removal of the solvent. Recrystallization from EtOAc–isopropyl ether gave a pure sample (10 mg) of C-nor-D-homocortisone 21-acetate (XIX), m.p. 203–204°; $[\alpha]_D^{22}$ +76° ($CHCl_3$); UV, λ_{max} 234 mμ (ε 16,800); IR, ν_{max} 3354, 1740, 1722, 1650, 1615, 1256, and 1232 cm^{-1}; NMR, τ 8·81 (3H, s, 19-Me), 8·72 (3H, d J = 6·2 c/s, 18-Me), 7·84 (3H, s, OAc), 5·20 and 4·90 (each 1H, q of AB type J = 17 c/s, 21-H), and 4·26 (1H, s, 4-H); ORD, $[\phi]$ values +820°, +100°, +185°, 0°, −5840°, −4540°, −4590°, 0°, and +8500° at 377, 367, 362, 359, 332, 324, 321, 309, and 278 mμ, respectively. (Found: C, 69·77: H, 7·56. $C_{23}H_{30}O_6$ requires: C, 69·54; H, 7·30%).

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