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12,13-Epoxy-*C*-nor-*D*-homosteroids. III.[1] The Synthesis and Stereochemistry of 17-Oxygenated 12,13-Epoxyetiojervanes[2]

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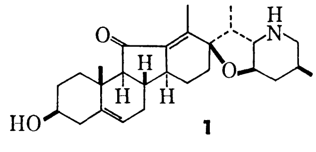
The synthesis of several 17-oxygenated 12,13-epoxyetiojervanes is described. Jervine (**1**) was degraded by a known procedure into trienone (**10**), which on hydride reduction afforded 11α- and 11β- alcohols (**11** and **12**). The respective alcohols were submitted to the Lemieux-Johnson oxidation to give Δ^{12}-17-oxo-11-alcohols (**13** and **14**), which were reduced under the Birch conditions to yield Δ^{12}-17-ketone (**15**). Epoxidation of these alcohols and ketone produced the aimed epoxides (**18**—**24**). The structure and configuration of these epoxides and the synthetic intermediates were determined on the basis of the chemical and spectral evidence.

In the previous papers[3)] we reported the synthesis and reaction of 11-oxygenated 17α-acetyl-12,13-epoxyetiojervanes. As a continuing study aimed at the preparation of biologically active normal steroids from jervine and other available alkaloids, we have been working on the synthesis and reaction of other types of 12,13-epoxyetiojervanes. In this Part we describe the synthesis and stereochemistry of 17-oxygenated 12,13-epoxyetiojervanes.

As the first step for the synthesis, it was undertaken to prepare 17-oxo-Δ^{12}-etiojervanes, important intermediates for the objective epoxy compounds. Jervine (**1**) was degraded by a known procedure, *via* trienone[4)] (**2a**), into Δ^{12}-11,17-diketone[5)] (**3**), which on treatment with zinc and acetic acid afforded 11,17-diketone[5)] (**4**), a known compound with established configurations,[6)] in a 67% yield together with a small amount (3%) of 11α-hydroxy-Δ^{12}-17-ketone (**5**), mp 249—250.5 °C. The α-hydroxy configuration at C_{11} of the latter (**5**) was deduced from facile conversion (82%) into its 3,11-diacetate (**5a**), mp 168—170 °C, under mild conditions. The major product (**4**) was then transformed, *via* the corresponding 17-ethylene acetal, amorphous, into a known compound, 3β-hydroxy-11,17-diketone 17-acetal[7)] (**6**), in an 81% yield, which on reduction with sodium in isopropyl alcohol gave 3β,11α-diol (**7**), mp 157—159 °C, in a 69% yield.



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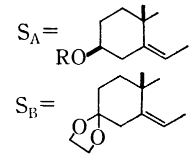
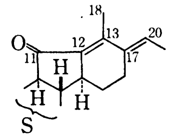
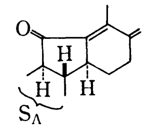
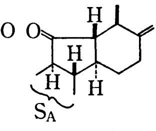




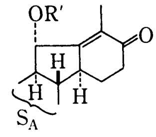
2 S=S_A, R=H
2a S=S_A, R=Ac
10 S=S_B



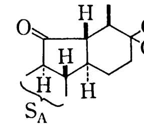
3 R=Ac



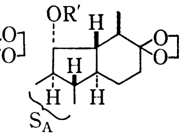
4 R=Ac



5 R=Ac, R′=H
5a R=R′=Ac

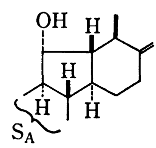


6 R=H
6a R=Ac

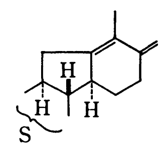


7 R=R′=H
7a R=Ac, R′=H
7b R=R′=Ac

The assigned α-configuration to the 11-hydroxyl group cf **7** was based on the chemical shift (δ 0.98) of the 19-methyl protons (δ_{calcd} 0.99 for 11α-OH and 1.26 for 11β-OH).[8)] Acetylation of 3β,11α-diol (**7**) under controlled conditions (0 °C, 1.5 h) effected monoacetylation to give, after chromatography, 3-monoacetate (**7a**), mp 235—236 °C, in a 57% yield with 3,11-diacetate (**7b**), mp 172—173 °C (12%), and the starting diol (**7**) (8%). The 3-monoacetate (**7a**) was smoothly deacetalized with *p*-toluenesulfonic acid in aqueous acetone to yield 17-ketone (**8**), mp 216.5—217.5 °C, and was also oxidized with chromic acid to 11-ketone (**6a**), mp 188—190 °C, in good yields, respectively. The latter (**6a**) proved to be identical with a known compound with established configurations,[6,7)] indicating that each of compounds **6**—**8** possesses a β-oriented hydrogen atom at C_{12}.



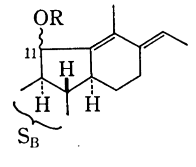
8 R=Ac



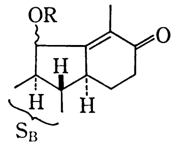
9 S=S_A, R=H
9a S=S_A, R=Ac
15 S=S_B

Compound **8**, 17-oxo-11α-alcohol, when treated with phosphoryl chloride and pyridine, underwent dehydration with concomitant double bond migration to give Δ^{12}-17-ketone (**9a**), mp 172—173 °C, in a low yield (38%), which was readily hydrolyzed with base (KOH) to the corresponding 3β-alcohol (**9**), mp 174—175 °C, quantitatively. In accordance with the formula, compound **9a** exhibited absorption maxima at 246 nm (ε 12000) and at 1665 cm^{-1} in the UV and IR spectra and displayed two three-proton singlets due to the 19- and 18-methyl protons at δ 1.04 and 1.73 in the NMR spectrum. This Δ^{12}-17-ketone (**9a**) was also obtained by treatment of 11α-acetoxy-Δ^{12}-17-ketone (**5a**) with zinc and acetic acid in a 73% yield. Likewise, 11α-hydroxy-17-ketone 17-acetal (**7a**), when treated with phosphoryl chloride under the same conditions as 17-ketone (**8**) and then with hydrochloric acid in aqueous dioxane, was converted into Δ^{12}-17-ketone (**9**) in a 74% yield. Compound **9** is one of the most important intermediates for preparation of the aimed 12,13-epoxides. However, the afore-mentioned process involved 11 steps and the over-all yield from jervine amounted to only 4%. In order to improve the yield of compound **9** or its analogues, we searched an alternate route.

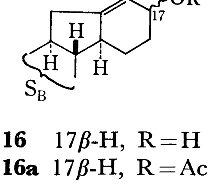
3β-Hydroxy-trienone[4] (**2**) was transformed *via* a known process into 3-oxo-trienone 3-acetal[9] (**10**), which was treated with aluminium hydride in tetrahydrofuran. The reduction proceeded without saturation of the double bonds[10] and, after chromatography, gave the corresponding 11α- and 11β-alcohols (**11** and **12**), mp 142—144 and 138—141 °C, in 59 and 21% yields, respectively. The configurations of C_{11} in these alcohols were assigned as shown in the formulas on the basis of chemical shifts of the protons at C_{19} and C_{11}; 19-CH_3, δ 1.10 for **11** and 1.30 for **12**;[3a,8] H at C_{11}, δ 4.66 (d $J=7$ Hz) for **11** and 4.90 (d $J=7$ Hz) for **12**.[3a] The result is interesting in the sense that the hydride reduction has led to predominant formation of 11α-alcohol (**11**), and we have such a precedent.[3a] The 11α-alcohol (**11**) was readily converted into its 11-acetate (**11a**), mp 171—174 °C, quantitatively, which on oxidation with sodium periodate in 75% aqueous dioxane (the Lemieux-Johnson oxidation)[11] afforded 11α-acetoxy-Δ^{12}-17-ketone (**13a**), mp 189—191 °C, in a 71% yield. This 17-ketone (**13a**) was also obtained by the Lemieux-Johnson oxidation of 11α-alcohol (**11**) into 11α-hydroxy-Δ^{12}-17-ketone (**13**), mp 186—188 °C, followed by acetylation in a 70% yield. Likewise, 11β-alcohol (**12**) was oxidized under the same conditions as **11** to give 11β-hydroxy-Δ^{12}-17-ketone (**14**), mp 169—170 °C in a 52% yield. These 11β-alcohols (**12** and **14**) were not converted into the respective 11-acetates under the same conditions as the corresponding 11α-alcohols (**11** and **13**). An attempted reduction to remove the oxygen functions at C_{11} of 11α-acetoxy- or 11β-hydroxy-Δ^{12}-17-ketone (**13a** or **14**) with zinc and acetic acid[12] produced a multi-component mixture containing 3-deacetalized compounds. However, the Birch reduction of these compounds (**13a** and **14**) effected the relevant reduction to give a desirable product, Δ^{12}-17-ketone (**15**), mp 163—165 °C, in 86 and 73% yields, respectively. The over-all yield of **15** amounted to 19%.



11 11β-H, R=H
11a 11β-H, R=Ac
12 11α-H, R=H



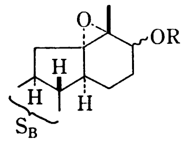
13 11β-H, R=H
13a 11β-H, R=Ac
14 11α-H, R=H



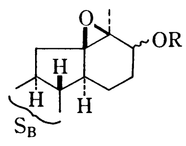
16 17β-H, R=H
16a 17β-H, R=Ac
17 17α-H, R=H
17a 17α-H, R=Ac

Reduction of Δ^{12}-17-ketone (**15**) with sodium borohydride produced Δ^{12}-17α-alcohol (**16**), mp 132—133 °C, in a 95% yield as a sole isolable compound. On the other hand, when aluminium hydride was used as the reduction reagent, its 17-epimer, Δ^{12}-17β-alcohol (**17**), mp 92—94 °C, was obtained in a 6% yield along with the 17α-epimer (**16**) (88%). The configurations of 17-hydroxyl groups were drawn from the optical rotations and spectral patterns of protons at C_{17}; $[\alpha]_D$ −25.7° for **16** and −77.3° for **17**;[13] H at C_{17}, δ 4.12 (br $W_H=18$ Hz) for **16** and 3.96 (br $W_H=8$ Hz) for **17**.[14] These Δ^{12}-17-alcohols (**16** and **17**) were readily transformed into the respective 17-acetates (**16a** and **17a**), mp 142—143 and 138—141 °C, quantitatively; H at C_{17}, δ 5.35 for **16a** and 5.21 for **17a**.[14] Prior to epoxidation of the 12,13-double bond, it was desirable to modify the Δ^5-3-ketone 3-acetal grouping into a Δ^4-3-carbonyl system, which leads to decrease of electrophilicity of the 5,6-double bond. However, all attempts to hydrolyze the 3-acetal group under various conditions (with *p*-toluenesulfonic acid in aqueous acetone under reflux or at room temperature, with anhydrous magnesium sulfate in wet benzene,[15] with trityl tetrafluoroborate in dry dichloromethane,[16] and so on) failed, giving complex mixtures. This suggested that the relevant epoxidation must be carried out under carefully controlled conditions.

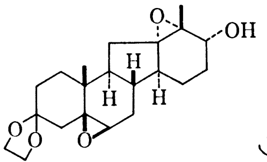
Epoxidation of Δ^{12}-17α-alcohol (**16**) with perbenzoic acid in benzene afforded 12α,13α-epoxy-17α-alcohol (**18**), mp 158—161 °C, as a main product (75%) with small amounts (3 and 6%) of 12β,13β-epoxy- and 5β,6β,12α,13α-diepoxy-17α-alcohols (**19** and **20**), mp 136—138 and 123—125 °C. The major product (**18**) was also obtained by oxidation of **16** with *t*-butyl hydroperoxide in the presence of bis(acetylacetonato)-oxovanadium(IV) in a 57% yield as a sole compound, which could be isolated from complex mixtures. The 12α,13α- and 12β,13β-epoxy configurations were assigned to compounds **18** and **19** on the premise that (i) peracid epoxidation of olefins takes place by an electrophilic attack mainly from a less-hindered (α) side,[17] and (ii) epoxidation of allyl alcohols in the presence of the transition metal leads to preferential formation of epoxides with the group at the same side as the hydroxyl group.[18] On the other hand, the epoxy-configurations of diepoxide (**20**) were deduced as shown by the formula from the chemical shift of 19-methyl protons; δ_{obsd} 0.99, δ_{calcd} 0.81 for 5α,6α,12α,13α-diepoxide and 1.02 for 5β,6β,12α,13α-diepoxide.[3a,8,19] Compound **18** was then converted into 17-acetate (**18a**), mp 212—213 °C, and oxidized with chromium(VI) oxide in pyridine to 12α,13α-epoxy-17-ketone (**21**), mp 139—140 °C, in good yields.[20] The latter (**21**) was also produced by direct oxidation of Δ^{12}-17-ketone (**15**) with hydrogen peroxide in alkaline aqueous methanol in an 86% yield. Reduction of the 17-ketone (**21**) produced two 17-epimeric alcohols, the original 17α-alcohol (**18**) and 12α,13α-epoxy-17β-alcohol (**22**), mp 144—146 °C, which were isolated in 65 and 25% yields from the mixture. The latter (**22**) readily formed 17-acetate (**22a**), mp 144—147 °C, quantitatively. The NMR spectra of these 17-epimeric alcohols were in good accord with the assigned configurations: H at C_{17}, δ 3.76 (br $W_H=28$ Hz) for **18** and 4.06 (br $W_H=7$ Hz) for **22**; δ 5.04 (do d $J=10$ and 5 Hz) for **18a** and 5.16 (br $W_H=6$ Hz) for **22a**.



18 17β-H, R=H
18a 17β-H, R=Ac
22 17α-H, R=H
22a 17α-H, R=Ac



19 17β-H, R=H
19a 17β-H, R=Ac
23 17α-H, R=H
23a 17α-H, R=Ac



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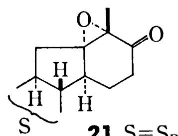
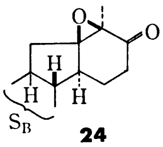


21 S=S_B
25 S=S_A, R=H



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Epoxidation of Δ^{12}-17β-alcohol (**17**) with *t*-butyl hydroperoxide in the presence of bis(acetylacetonato)-oxovanadium(IV)[18] proceeded smoothly to give a new epoxide, 12β,13β-epoxy-17β-alcohol (**23**), mp 130—132 °C, in an 83% yield, which formed 17-acetate (**23a**), mp 132—135 °C, in a good yield. Oxidation of **23** with chromium(VI) oxide in pyridine afforded 12β,13β-epoxy-17-ketone (**24**), mp 184—186 °C, in an 80% yield, which was reconverted by treatment with sodium borohydride into the original 17β-alcohol (**23**) only in a 38% yield, the major product being 12β,13β-epoxy-17α-alcohol (50%). The latter was readily converted into 17-acetate (**19a**), mp 142—144 °C, and was naturally identical with the afore-mentioned epoxy-alcohol (**19**). A series of these reactions correlating all 17-hydroxy- and 17-oxo-12,13-epoxides (**18**—**24**) were consistent with the assigned epoxy configurations to the respective compounds. Confirmatory evidence was presented by comparison of the ORD curves of two epoxy-ketones (**21** and **24**), which exhibited negative and positive Cotton effects ($a=-119°$ and $+125°$), respectively (Fig. 1).

Finally we examined collectively the chemical shifts of 19-methyl protons of etiojervanes described in this paper. We now add the contributions of new functional groups shown in Table 1 to *Table 2 in the Ref. 8.* These data, coupled with those in *Table 1 of the Ref. 3a,* would be valuable in confirming certain stereochemical points as well as promoting the structure determination of new derivatives. For example, 3β-hydroxy-Δ^{12}-17-ketone (**9**) was oxidized with hydrogen peroxide in an alkaline solution to give 12α,13α-epoxy-17-ketone (**25**), mp 173.5—175 °C, in a 57% yield. This epoxide (**25**) exhibited the ORD curve with a negative Cotton effect ($a=-99°$) and the NMR signal due to the 19-methyl protons at δ 1.02; δ_{calcd} 1.00 for 12α,13α-epoxide and 1.09 for 12β,13β-epoxide.

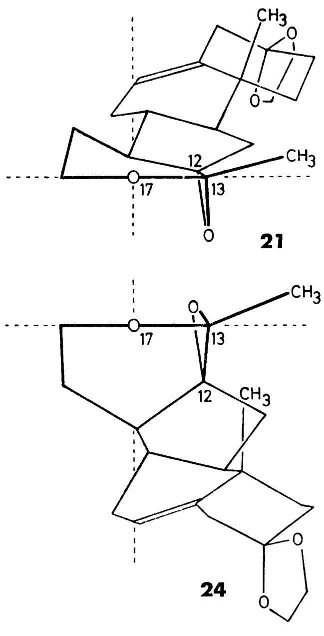

Fig. 1.

TABLE 1. THE CONTRIBUTION ($\Delta\delta$) OF FUNCTIONAL GROUPS TO THE CHEMICAL SHIFT OF THE 19-METHYL PROTONS OF ETIOJERVANES

Groups		A-T[a]	B-T[a]
Reference shifts		0.74[a]	0.79[a]
Functional groups (No of examples)		$\Delta\delta$[b]	$\Delta\delta$[b]
11β-OH, Δ^{12}, $\Delta^{17(20)}$	(1)	0.32	—
11α-OH, Δ^{12}, $\Delta^{17(20)}$	(1)	0.12	—
11α-OAc, Δ^{12}, $\Delta^{17(20)}$	(1)	0.16	—
11β-OH, Δ^{12}, 17=O	(1)	0.34	—
11α-OH, Δ^{12}, 17=O	(2)	0.16	—
11α-OAc, Δ^{12}, 17=O	(2)	0.20	—
12β,13β-O-[c]	(5)	0.06	—
12α,13α-O-[c]	(5)	—	−0.01[d]
12β,13β-O-, 17=O	(1)	0.12	—
12α,13α-O-, 17=O	(2)	—	−0.02[d]

a) *Cf.*, Table 2 in Ref. 8. b) "$\Delta\delta$" means deshielding effect. c) The abbreviations "12β,13β-O- and 12α, 13α-O-" denote "12β,13β-epoxy and 12α,13α-epoxy", respectively. d) The negative sign means "up-field shift".

Experimental

All the mps were uncorrected. The homogenity of each compd was always checked by TLC over silica gel (Wakogel B-5) with various solvent systems, and the spots were developed with cerium(IV) sulfate in dil sulfuric acid and/or iodine. The optical rotations, ORD curves, UV and IR spectra were measured in chloroform, dioxane, ethanol, and Nujol, respectively, unless otherwise stated. The NMR spectra were obtained in chloroform-*d* at 100 MHz, and the chemical shifts were given in δ-values, TMS being used as an internal reference. The abbreviations "s, d, t, q, br, do, and sh" in the NMR and IR spectra denote "singlet, doublet, triplet, quartet, broad, double, and shoulder," respectively.

*3β-Hydroxy-12β-etiojerv-5-ene-11,17-dione 3-Acetate (**4**), 3β,-11α-Dihydroxyetiojerva-5,12-dien-17-one 3-Acetate (**5**), and Its 3,11-Diacetate (**5a**).* A soln of 3β-hydroxyetiojerva-5,-12-diene-11,17-dione 3-acetate[5] (**3**, 22 g) in glacial acetic acid (1730 ml) was heated with zinc powder (27.5 g) at 90 °C for 30 min under stirring, when the yellow soln had become colorless. The reaction mixture was worked up according to the known procedure[5] to give crystalline residue (32 g), showing two spots, which was separated by chromatography over alumina (Merck, standard, 340 g). Eluates with benzene-hexane (3 : 1), benzene, and benzene-ether (3 : 1) afforded **4** (14.8 g), mp 164—166 °C (diisopropyl ether) (lit,[4] 171—172 °C). Eluates with chloroform gave **5** (0.66 g), mp 246—248 °C (acetone), which was recrystallized from acetone for analysis; mp 249—250.5 °C and $[\alpha]_D$ −61°; MS, *m/e* 344 (M^+); UV, λ_{max} 249 nm (ε 15000); IR, ν_{max} 3495, 1722, 1648 (br), 1250, 1041, and 1031 cm^{-1}; NMR, δ 1.14, 1.90, and 2.07 (each 3H, s, 19- and 18-C$\underline{H}_3$, and OCOC$\underline{H}_3$), 4.67 (1H, br W_H=24 Hz, $\underline{H}$ at C_3), 4.73 (1H, d J=7 Hz, $\underline{H}$ at C_{11}), and 5.46 (1H, br W_H=10 Hz, $\underline{H}$ at C_6). Found: C, 73.24; H, 8.19%. Calcd for $C_{21}H_{28}O_4$:C, 73.22; H, 8.19%.

A soln of **5** (1.44 g) in acetic anhydride (Ac_2O, 7.2 ml) and pyridine (Py, 14.4 ml) was allowed to stand at room temp for 24 h. The reaction mixture was poured into ice-water and extracted with chloroform. The chloroform soln was washed with 2 M hydrochloric acid, 5% aq sodium hydrogencarbonate and water, dried over anhyd sodium sulfate, and evaporated to leave amorphous residue (2.02 g), which was crystallized from acetone to yield **5a** (1.33 g), mp 167—170 °C. This was recrystallized for analysis from acetone; mp 168—170 °C and $[\alpha]_D$ −93°; MS, *m/e* 326 (M^+-CH_3COOH), 284, 266, and 251; UV, λ_{max} 244 nm (ε 15000); IR ν_{max} 1724, 1670, 1249, 1238, 1042, and 1033 cm^{-1}; NMR, δ 1.19 and 1.68 (each 3H, s, 19- and 18-C$\underline{H}_3$), 2.05 and 2.07 (each 3H, s, 2OCOC$\underline{H}_3$), 4.63, and 5.47 (each 1H, br W_H=22 and 9.5 Hz, 2$\underline{H}$ at C_3 and C_6), and 6.12 (1H, d J=8 Hz, $\underline{H}$ at C_{11}). Found: C, 71.38: H, 7.81%. Calcd for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82%.

*3β-Hydroxy-12β-etiojerv-5-ene-11,17-dione 17-Ethylene Acetal (**6**).* A soln of **4** (20 g) in ethylene glycol (80 ml) was refluxed with *p*-toluenesulfonic acid (PTS, 1.0 g) in benzene (1600 ml) for 21 h, water being removed with a Dean-Stark apparatus. After being cooled, the soln was worked up as usual to leave crude acetal (23.7 g), which, without purification, was refluxed in methanol (670 ml) containing potassium hydroxide (70 g) for 1 h under nitrogen. The reaction mixture was worked up as usual to leave crystalline residue, which was recrystallized from hexane-benzene to give **6** (16.3 g), mp 160—162 °C (lit,[7] 165—167 °C).

*3β,11α-Dihydroxy-12β-etiojerv-5-en-17-one 17-Ethylene Acetal (**7**), Its 3-Acetate (**7a**), and 3,11-Diacetate (**7b**).* To a refluxing soln of **6** (10.0 g) in isopropyl alcohol (1400 ml) was added in small protions sodium metal (51 g) during 2 h. The mixture was further refluxed for 20 min under stirring, when it had become homogeneous. After being cooled, the mixture was combined with water (300 ml) and concentrated under reduced pressure to leave oily residue, which was mixed with water and extracted with chloroform. The extracts were worked up as usual to leave amorphous residue, which on trituration with aq ethanol afforded **7** (6.98 g), mp 156—158 °C. This was recrystallized from the same solvent mixture for analysis; mp 157—159 °C and $[\alpha]_D$ −34°; MS, *m/e* 348 (M^+), 330, 315, 286, and 259; IR, ν_{max} 3370, 1089, and 1050 cm^{-1}; NMR, δ 0.94 (3H, d J=7 Hz, 18-C$\underline{H}_3$), 0.98 (3H, s, 19-C$\underline{H}_3$), 3.48 (1H, br W_H=26 Hz, $\underline{H}$ at C_3), 3.94 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 4.05 and 5.32 (each 1H, br W_H=8 and 10 Hz, 2$\underline{H}$ at C_{11} and C_6). Found: C, 70.65; H, 9.39%. Calcd for $C_{21}H_{32}O_4\cdot C_2H_5OH$: C, 70.01; H, 9.71%.

Compd **7** (125 mg) was dissolved in Py (1.26 ml) and Ac_2O (0.33 ml) under cooling with ice and then allowed to stand at room temp for 1.5 h. After being poured into ice-water, the mixture was extracted with chloroform. The extracts were worked up as usual to leave oily residue (164 mg), showing three spots on TLC, which was separated by chromatography over silica gel (Merck, 9 g). Eluates with benzene-ether (5 : 1) were crystallized and recrystallized from hexane to give **7b** (18 mg), mp 172—173 °C and $[\alpha]_D$ −15°; MS, *m/e* 432 (M^+), 372, 357, 312, and 297; IR, ν_{max} 1731, 1240 (br), 1086, 1043, and 1018 cm^{-1}; NMR, δ 0.77 (3H, d J=6 Hz, 18-C$\underline{H}_3$), 1.07 (3H, s, 19-C$\underline{H}_3$), 2.00 and 2.02 (each 3H, s, 2OCOC$\underline{H}_3$), 3.92 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 4.53 (1H, br W_H=20 Hz, $\underline{H}$ at C_3), and 5.37 (2H, br W_H=10 Hz, 2$\underline{H}$ at C_{11} and C_6). Found: C, 69.24; H, 8.27%. Calcd for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39%.

Eluates with benzene-ether (3 : 1) were crystallized and recrystallized from diisopropyl ether to give **7a** (80 mg), mp 235—236 °C and $[\alpha]_D$ −43°; MS, *m/e* 390 (M^+), 330, 268, and 242; IR, ν_{max} 3540, 1725, 1253, 1085, 1035, and 1023 cm^{-1}; NMR, δ 0.95 (3H, d J=6.5 Hz, 18-C$\underline{H}_3$), 1.00 (3H, s, 19-C$\underline{H}_3$), 2.01 (3H, s, OCOC$\underline{H}_3$), 3.94 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O) 4.10, 4.60, and 5.38 (each 1H, br W_H=9, 22, and 9 Hz, 3H at C_{11}, C_3, and C_6). Found: C, 70.84; H, 8.83%. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78%. Eluates with benzene-ether (1 : 1) were crystallized and recrystallized from aq ethanol to give the starting material (**7**, 10 mg), mp 156—158 °C, which was identical with an authentic sample.

To a pasty mixture, prepared by addition of chromium(VI) oxide (500 mg) into Py (5 ml) at 0 °C under stirring, was added a soln of **7a** (20 mg) in Py (0.8 ml), and the whole mixture was stirred at room temp for 22 h. The reaction mixture was worked up as usual to yield an oily material, which was purified by chromatography over silica gel (Merck, 1 g). Eluates with benzene–ether (5 : 1) afforded 12β-etiojerv-5-en-3β-ol-11,17-dione 3-acetate 17-ethylene acetal (**6a**, 10 mg), mp 188—190 °C (diisopropyl ether), which was identical with an authentic sample[6,7] (IR, NMR, TLC, and mixed mp).

*3β,11α-Dihydroxy-12β-etiojerv-5-en-17-one 3-Acetate (**8**).* A soln of **7a** (1.91 g) in acetone (300 ml) and water (30 ml) was refluxed with PTS (150 mg) for 3 h under stirring. The soln was worked up as usual to leave crystalline residue (1.68 g), showing a single spot, which was recrystallized from acetone to give **8** (1.61 g), mp 216.5—217.5 °C and $[\alpha]_D$ −139°; MS, *m/e* 286 (base, M^+ $-CH_3COOH$), 271, 268, and 253; IR, ν_{max} 3615, 1728, 1696, 1250, and 1036 cm^{-1}; NMR, δ 1.03 (3H, s, 19-C$\underline{H}_3$), 1.11 (3H, d J=6 Hz, 18-C$\underline{H}_3$), 2.06 (3H, s, OCOC$\underline{H}_3$), 4.13 (1H, do d J=4 and 6 Hz, $\underline{H}$ at C_{11}), 4.63 and 5.43 (each 1H, br W_H=23 and 9 Hz, 2$\underline{H}$ at C_3 and C_6). Found: C, 72.97; H, 8.73%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

*3β-Hydroxyetiojerva-5,12-dien-17-one 3-Acetate (**9a**).* (i) Compd **5a** (204 mg), dissolved in glacial acetic acid (14 ml), was stirred vigorously with zinc powder (440 mg) at 90 °C for 30 min. The mixture, after being cooled, was filtered to remove excess of the zinc powder, which was washed with chloroform. The filtrate and chloroform washings were combined, evaporated, diluted with water, and then extracted with chloroform. The extracts were worked up as usual to leave an amorphous substance (172 mg), which was crystallized from acetone to yield **9a** (127mg), mp 172—173 °C. This was recrystallized for analysis from acetone; mp 172—173 °C and $[\alpha]_D$ −93.4°; MS, *m/e* 328 (M^+), 268, 253; UV, λ_{max} 246 nm (ε 12000); IR, ν_{max} 1731, 1665, 1248, and 1035 cm^{-1}; NMR, δ 1.04, 1.73, and 2.05 (each 3H, s, 19- and 18-C$\underline{H}_3$, and OCOC$\underline{H}_3$), 4.66 and 5.45 (each 1H, br W_H=21 and 9 Hz, 2$\underline{H}$ at C_3 and C_6). Found: C, 76.96; H, 8.52%. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59%.

(ii) To a soln of **8** (1.5 g) in dry Py (39 ml), cooled at 0 °C, was added dropwise phosphoryl chloride ($POCl_3$, freshly distilled, 1.95 ml) during 1 min under stirring, and the mixture was kept at room temp for 9 min. The reaction mixture was poured into ice–water (*ca.* 500 ml) and extracted with chlorofrom, and the chloroform soln was worked up as usual to give a crystalline substance, which was recrystallized from acetone to give **9a** (540 mg), mp 172—173 °C, identical with an authentic sample.

*3β-Hydroxyetiojerva-5,12-dien-17-one (**9**).* (i) Compd **9a** (6.49 g) was refluxed in methanol (160 ml) containing 5% potassium hydroxide for 1 h under nitrogen. The reaction mixture was worked up as usual to leave a crystalline substance (6.04 g), which was purified by chromatography over silica gel (Merck, 60 g). Eluates with benzene - ether (1 : 3) afforded **9** (5.07 g), mp 172—174 °C (acetone), which was recrystallized for analysis from acetone; mp 174—175 °C and $[\alpha]_D$ −106°; MS, *m/e* 286 (M^+), 268, and 253; UV, λ_{max} 246 nm (ε 12000); IR, ν_{max} 3440, 1643, and 1065 cm^{-1}; NMR, δ 1.03 and 1.73 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.57 and 5.42 (each 1H, br W_H=23 and 9 Hz, 2$\underline{H}$ at C_3 and C_6). Found: C, 79.70; H, 9.14%. Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15%.

(ii) A soln of **7a** (5.68 g) in Py (57 ml) was treated with $POCl_3$ (5.7 ml) at room temp for 12 min (*cf.*, dehydration of **8**). The reaction mixture was worked up as mentioned above to leave an amorphous material (5.62 g), which was dissolved in dioxane (300 ml) and water (110 ml), and treated with concd hydrochloric acid (25 ml) at room temp for 25 h under stirring. The mixture was concentrated to 200 ml below 65 °C under reduced pressure, diluted with water, and then allowed to stand overnight, when crystalline substances (3.75 g) precipitated. These were collected by filtration and recrystallized from acetone to yield **9** (3.09 g), mp 169—170 °C, identical with an authentic sample.

*11α-Hydroxy-17-ethyletiojerva-5,12,17(20)-trien-3-one 3-Ethylene acetal (**11**), Its 11-Acetate (**11a**), and Its 11β-Ol Epimer (**12**).* (i) To an ice-cooled, stirred suspended mixture of lithium aluminium hydride (LAH, 3.40 g) in dry tetrahydrofuran (THF, 120 ml) was added dropwise 95% sulfuric acid (2.3 ml) under a stream of nitrogen, and the mixture was further stirred at room temp for 1 h and then kept in a refrigerator. The supernatant THF soln contained 0.75 M aluminium hydride. To a soln of 17-ethyletiojerva-5,12,17(20)-triene-3,11-dione 3-ethylene acetal[9] (**10**, 5.0 g) in THF (60 ml) cooled with ice was added slowly the above THF soln (25 ml) under stirring, and the whole mixture was stirred at room temp for 3 h. After addition of ethanol and 6 M aq ammonia to decompose excess of the hydride, the reaction mixture was filtered to remove aluminium hydroxide, which was washed with ethanol. The filtrate and ethanol washings were combined, concentrated, diluted with water, and extracted with chloroform. The extracts were washed with water, dried, and evaporated to leave oily residue, which was separated by chromatography over alumina (Merck, 200 g). Eluates with benzene-ether (3 : 1 and 2 : 1) gave the starting trienone (**10**, 77 mg). Eluates with benzene-ether (1 : 1) afforded crystalline substances, which were collected by filtration and recrystallized from benzene-ether to yield **12** (1.06 g), mp 138—141 °C and $[\alpha]_D$ −2.0°; MS, *m/e* 356 (M^+), 341, 338, and 323; UV, λ_{max} 260 (sh), 252, and 244 (sh) nm (ε 7000, 11000, and 10000); IR, ν_{max} 3540, 1110, and 1095 cm^{-1}; NMR, δ 1.30 and 1.93 (each 3H, s, 19- and 18-C$\underline{H}_3$), 1.72 (3H, d *J*=7 Hz, 21-C$\underline{H}_3$), 3.96 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 4.90 (1H, d *J*=7 Hz, $\underline{H}$ at C_{11}), 5.30 (1H, br W_H=11 Hz, $\underline{H}$ at C_6), and 5.60 (1H, q *J*=7 Hz, $\underline{H}$ at C_{20}). Found: C, 77.54; H, 8.99%. Calcd for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05%.

Eluates with ether afforded **11** (2.96 g), mp 142—144 °C and $[\alpha]_D$ +6.9°; MS, *m/e* 356 (M^+), 341, 338, 323, and 239; UV, λ_{max} 258 (sh), 250, and 242 (sh) nm (ε 7000, 10000, and 9000); IR, ν_{max} 3350, 1110, and 992 cm^{-1}; NMR, δ 1.10 and 1.90 (each 3H, s, 19- and 18-C$\underline{H}_3$), 1.72 (3H, d *J*=7 Hz, 21-C$\underline{H}_3$), 3.96 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 4.66 (1H, d *J*=7 Hz, $\underline{H}$ at C_{11}), 5.36 (1H, br W_H=11 Hz, $\underline{H}$ at C_6), and 5.56 (1H, q *J*=7 Hz, $\underline{H}$ at C_{20}). Found: C, 77.58; H, 9.10%. Calcd for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05%.

(ii) Compd **11** (205 mg) was treated with Ac_2O (1 ml) and Py (2 ml) at room temp overnight under stirring. The reaction mixture was worked up as usual to give **11a** (228 mg), mp 171—174 °C (benzene-ether) and $[\alpha]_D$ −37.5°; MS, *m/e* 398 (M^+), 338, and 323; UV, λ_{max} 259 (sh), 250, and 244 (sh) nm (ε 9500, 14800, and 13600); IR, ν_{max} 1720, 1245, 1108, and 1092 cm^{-1}; NMR, δ 1.16 and 1.72 (each 3H, s, 19- and 18-C$\underline{H}_3$), 1.69 (3H, d *J*=7 Hz, 21-C$\underline{H}_3$), 2.03 (3H, s, OCOC$\underline{H}_3$), 3.96 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 5.37 (1H, br W_H=12 Hz, $\underline{H}$ at C_6), 5.60 (1H, q *J*=7 Hz, $\underline{H}$ at C_{20}), and 6.10 (1H, d *J*=7 Hz, $\underline{H}$ at C_{11}). Found: C, 75.01; H, 8.43%. Calcd for $C_{25}H_{34}O_4$: C, 75.34; H, 8.60%.

*11α-Hydroxyetiojerva-5,12-diene-3,17-dione 3-Ethylene Acetal (**13a**) and Its 11-Acetate (**13a**).* (i) A soln of **11a** (850 mg) in 75% aq dioxane (70 ml) was stirred with osmium tetraoxide in dioxane (0.74 ml) (OsO_4 : dioxane = 1.0 g : 80 ml) at room temp for 30 min, when the colorless soln gradually became dark-brown. To the soln was added sodium periodate (0.88 g) during 30 min, and the mixture was stirred at room temp for 22 h, when white precipitates separated out and were removed by filtration. The filtrate was concentrated, diluted with water, and extracted with chloroform repeatedly. The chloroform soln was washed with water, dried and evaporated to leave amorphous residue, which was purified by chromatography over silica gel (Merck, 34 g) with mixtures of benzene and ether to give **13a** (584 mg), mp 189—191 °C (benzene-ether) and $[\alpha]_D$ −79.7°; MS, *m/e* 386 (M^+) and 326; UV, λ_{max} 244 nm (ε 11000); IR, ν_{max} 1732, 1658, 1240, and 1093 cm^{-1}; NMR, δ 1.18, 1.66, and 2.06 (each 3H, s, 19- and 18-C$\underline{H}_3$, and OCOC$\underline{H}_3$), 3.97 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 5.40 (1H, br W_H=9 Hz, $\underline{H}$ at C_6), and 6.10 (1H, d *J*=7 Hz, $\underline{H}$ at C_{11}). Found: C, 71.03; H, 7.38%. Calcd for $C_{23}H_{30}O_5$: C, 71.48; $\underline{H}$, 7.82%.

(ii) Compd **11** (2.20 g) was oxidized in the same manner as **11a** to give **13** (1.48 g), mp 186—188 °C (benzene-ether) and $[\alpha]_D$ −44.1°; MS, *m/e* 344 (M^+); UV, λ_{max} 249 nm (ε 12000); IR, ν_{max} 3480, 1665, 1110, and 1095 cm^{-1}; NMR, δ 1.14 and 1.90 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.98 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 4.78 (1H, d *J*=7 Hz, $\underline{H}$ at C_{11}), and 5.43 (1H, br W_H=10 Hz, $\underline{H}$ at C_6). Found: C, 73.30; H, 8.10%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

Compd **13** (4.16 g) was treated with Ac_2O (21 ml) and Py (42 ml) at room temp overnight under stirring to give **13a** (4.64 g), which was identical with an authentic sample.

*11β-Hydroxyetiojerva-5,12-diene-3,17-dione 3-Ethylene Acetal (**14**).* The Lemieux-Johnson oxidation of **12** (105 mg) was carried out in the same manner as that of **11** and gave **14** (51 mg), mp 169—170 °C (benzene-ether); MS, *m/e* 344

(M^+); UV, λ_{max} 247 nm (ε 10600); IR, ν_{max} 3360, 1640, 1118, and 1100 cm^{-1}; NMR, δ 1.32 and 1.90 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.98 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 5.00 (1H, d J=7 Hz, $\underline{H}$ at C_{11}), and 5.30 (1H, br W_H =10 Hz, $\underline{H}$ at C_6). Found: C, 73.45; H, 8.40%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

Etiojerva-5,12-diene-3,17-dione 3-Ethylene Acetal (**15**). (i) To a blue-colored soln of lithium (2.0 g) in liquid ammonia (*ca.* 300 ml) cooled with Dry Ice-Acetone was added **13a** (4.7 g) in THF (15 ml), and the mixture was stirred at the temp for 15 min. The reaction mixture, on addition of ammonium chloride (20 g), became colorless and was then allowed to stand at room temp to remove the ammonia. The residue was submitted to filtration to remove ammonium chloride, the latter being washed with ethanol. The filtrate and ethanol washings were combined, concentrated, diluted with water, and extracted with chloroform, repeatedly. The extracts were worked up as usual to give crystalline residue, which on recrystallization from ether yielded **15** (3.43 g), mp 163—165 °C and $[\alpha]_D$ −81.5°; MS, *m/e* 328 (M^+); UV, λ_{max} 247 nm (ε 9200); IR, ν_{max} 1658 and 1110 cm^{-1}; NMR, δ 1.06 and 1.73 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.98 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), and 5.42 (1H, br W_H=10 Hz, $\underline{H}$ at C_6). Found: C, 76.65; H, 8.68%. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59%.

(ii) The Birch reduction of **14** (8.00 g) was carried out in the same manner as that of **13a** and produced **15** (5.58 g), which was identical with the afore-mentioned sample.

17α-Hydroxyetiojerva-5,12-dien-3-one 3-Ethylene Acetal (**16**), *Its 17β-Ol Epimer* (**17**), *and Their 17-Acetates* (**16a** *and* **17a**). (i) A soln of **15** (1.00 g) in methanol (100 ml) was stirred with sodium borohydride (1.8 g) at room temp for 35 min. After addition of a small amount of acetic acid, the mixture was neutralized with 5% aq sodium hydrogencarbonate, concentrated, diluted with water, and extracted with chloroform, repeatedly. The chloroform soln gave crystalline residue, which was recrystallized from ether to yield **16** (950 mg), mp 132—133 °C and $[\alpha]_D$ −25.7°; MS, *m/e* 330 (M^+) and 312; IR, ν_{max} 3360, 1110, and 1090 cm^{-1}; NMR, δ 0.98 and 1.65 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.94 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 4.12 and 5.35 (each 1H, br W_H=18 and 10 Hz, 2$\underline{H}$ at C_{17} and C_6). Found: C, 75.93; H, 9.12%. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15%.

Compd **16** (0.11 g) was treated with Ac_2O (0.7 ml) and Py (1.4 ml) at room temp for 1 d under stirring to give **16a** (0.12 g), mp 142—143 °C (benzene-ether) and $[\alpha]_D$ −10.6°; MS, *m/e* 372 (M^+) and 312; IR, ν_{max} 1734, 1237, 1107, 1092, 1019, and 976 cm^{-1}; NMR, δ 0.99, 1.54, and 2.06 (each 3H, s, 19- and 18-C$\underline{H}_3$, and OCOC$\underline{H}_3$), 3.94 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), and 5.35 (2$\underline{H}$, br W_H=10 Hz, 2$\underline{H}$ at C_6 and C_{17}). Found: C, 74.05; H, 8.62%. Calcd for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66%.

(ii) To an ice-cooled and stirred soln of LAH (0.8 g) in THF (40 ml) was added dropwise concd sulfuric acid (0.7 ml) under a stream of nitrogen, and the mixture was then kept in a refrigerator. To a soln of **15** (2.00 g) in THF (20 ml) was added slowly the above supernatant THF soln (25 ml) under nitrogen, and the whole mixture was stirred at room temp for 2 h. The mixture, after being worked up as described before, gave amorphous residue, which was separated by chromatography over silica gel (Merck, 65 g). Eluates with benzene-ether (2 : 1) afforded a mixture, showing two spots, which was further separated by preparative TLC over silica gel (Wakogel B-5, 35 plates of 20×20 cm^2) with benzene-ether (2 : 1). A less polar fraction afforded **17** (0.11 g), mp 92—94 °C (benzene-ether) and $[\alpha]_D$ −77.3°; MS, *m/e* 330 (M^+), 312, and 297; IR, ν_{max} 3500, 3260, 1190, 1035, 1015, and 970 cm^{-1}; NMR, δ 0.98 and 1.71 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.94 (5H, s, OC$\underline{H}_2$C$\underline{H}_2$O and $\underline{H}$ at C_{17}), and 5.36 (1H, br W_H=10 Hz, $\underline{H}$ at C_6). Found: C, 75.93; H, 9.34%. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15%. A more polar fraction afforded **16** (1.77 g), which was obtained from eluates with benzene-ether (1 : 1) and ether, and proved to be identical with an authentic sample.

Compd **17** (14 mg) was acetylated with Ac_2O (0.4 ml) and Py (0.8 ml) at room temp for 3 d to give **17a** (15 mg), mp 138—141 °C (acetone) and $[\alpha]_D$ −89.7°; MS, *m/e* 372 (M^+) and 312; IR, ν_{max} 1738, 1238, 1108, 1090, 1020, and 957 cm^{-1}; NMR, δ 1.00, 1.59, and 2.05 (each 3H, s, 19- and 18-C$\underline{H}_3$, and OCOC$\underline{H}_3$), 3.95 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 5.21 and 5.39 (each 1H, br W_H=8 and 10 Hz, 2$\underline{H}$ at C_{17} and C_6). Found: C, 74.18; H, 8.63%. Calcd for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66%.

Epoxidation of **16**. (i) To a soln of **16** (100 mg) in dry benzene (10 ml) was added perbenzoic acid (50 mg, purity 95%), and the mixture was stirred at room temp for 30 min. After addition of 5% aq sodium thiosulfate, the mixture was concentrated and shaken with water and chloroform. The chloroform soln was washed with 5% aq sodium hydrogencarbonate and water, dried and evaporated to leave amorphous residue, which was separated by chromatography over silica gel (Merck, 4.0 g). Eluates with benzene-ether (3 : 1) gave a crystalline substance (4 mg), which was recrystallized from benzene to give 17α-hydroxy-12β,13β-epoxyetiojerv-5-en-3-one 3-ethylene acetal (**19**), mp 136—138 °C and $[\alpha]_D$ −63.8°; MS, *m/e* 346 (M^+) and 328; IR, ν_{max} 3500, 1106, and 1022 cm^{-1}; NMR, δ 1.04 and 1.40 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.96 (5H, s, OC$\underline{H}_2$C$\underline{H}_2$O and $\underline{H}$ at C_{17}), and 5.36 (1H, br W_H=10 Hz, $\underline{H}$ at C_6). Found: C, 72.48; H, 8.75%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

Eluates with benzene-ether (2 : 1) gave the 12α,13α-epoxy epimer (**18**, 75 mg), which was recrystallized for analysis from benzene-ether: mp 158—161 °C and $[\alpha]_D$ −57.0°; MS, *m/e* 346 (M^+) and 328; IR, ν_{max} 3440, 1110, 1100, and 1035 cm^{-1}; NMR, δ 1.00 and 1.40 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.76 (1H, br W_H=28 Hz, $\underline{H}$ at C_{17}), 3.96 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), and 5.38 (1H, br W_H=11 Hz, $\underline{H}$ at C_6). Found: C, 72.89; H, 8.74%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. Eluates with benzene-ether (1 : 1) afforded the 5β,6β,12α,13α-diepoxide (**20**, 10 mg), mp 123—125 °C (benzene-ether) and $[\alpha]_D$ −28.6°; MS, *m/e* 362 (M^+) and 347; IR, ν_{max} 3460, 1100, 1040, and 957 cm^{-1}; NMR, δ 0.99 and 1.38 (each 3H, s, 19- and 18-C$\underline{H}_3$), 3.14 and 3.72 (each 1H, br W_H=5 and 24 Hz, 2$\underline{H}$ at C_6 and C_{17}), and 3.90 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O). Found: C. 69.44; H, 8.43%. Calcd for $C_{21}H_{30}O_5$: C, 69.58; H, 8.34%.

Compd **18** (300 mg) and **19** (10 mg) were treated with Ac_2O and Py (1.5 and 3 ml, and 0.15 and 0.3 ml) to give the respective acetates (**18a**, 276 mg and **19a**, 8 mg). Compd **18a**, mp 212—213 °C (acetone) and $[\alpha]_D$ −44.7°; MS, *m/e* 388 (M^+) and 328; IR, ν_{max} 1737, 1240, 1107, 1092, and 1030 cm^{-1}; NMR, δ 1.00, 1.26, and 2.12 (each 3H, s, 19- and 18-C$\underline{H}_3$, and OCOC$\underline{H}_3$), 3.96 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 5.04 (1H, do d J=5 and 10 Hz, $\underline{H}$ at C_{17}), and 5.37 (1H, br W_H=10 Hz, $\underline{H}$ at C_6). Found: C, 70.82; H, 8.31%. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30%. Compd **19a**, mp 142—144 °C (ether) and $[\alpha]_D$ −53.0°; MS, *m/e* 388 (M^+) and 328; IR ($CHCl_3$), ν_{max} 1732, 1248, 1110, 1095, and 1025 cm^{-1}; NMR, δ 1.04, 1.29, and 2.06 (each 3H, s, 19- and 18-C$\underline{H}_3$, and OCOC$\underline{H}_3$), 3.96 (4H, s, OC$\underline{H}_2$C$\underline{H}_2$O), 5.04 and 5.37 (each 1H, br W_H=14 and 10 Hz, 2$\underline{H}$ at C_{17} and C_6). Found: C, 70.34; H, 8.83%. Calcd for $C_{23}H_{32}O_5$·

0.5 $(C_2H_5)_2O$: C, 70.56; H, 8.76%.

(ii) To a refluxing, green-colored soln of **16** (200 mg) in dry benzene (3 ml) containing bis(acetylacetonato)oxovanadium(IV) (2.7 mg) was added rapidly *t*-butyl hydroperoxide (0.12 ml), when the soln became yellow-colored. The soln was then refluxed for 20 min and cooled. The reaction mixture was washed with 5% aq sodium hydrogensulfite, until the mixture became colorless, and then with water, dried and evaporated to leave a resinous material, which was purified by chromatography over silica gel (Merck, 8.0 g) to yield **18** (120 mg), mp 157—159 °C, from eluates with benzene–ether (1 : 2). This was identical with the afore-mentioned sample.

*12α,13α-Epoxyetiojerv-4-ene-3,17-dione 3-Ethylene Acetal (**21**).* (i) A soln of **15** (200 mg) in methanol (14 ml), containing 4 M aq sodium hydroxide (0.4 ml) and 30% aq hydrogen peroxide (0.8 ml), was allowed to stand in a refrigerator for 3 d. The reaction mixture was concentrated and shaken with water and chloroform, and the chloroform soln was washed with 5% aq sodium thiosulfate and water, dried and evaporated to give amorphous residue, which was purified by chromatography over silica gel (Merck, 7.0 g). Eluates with benzene–ether (2 : 1) gave a crystalline substance, which was recrystallized from benzene–ether to give **21** (180 mg), mp 139—140 °C and $[\alpha]_D$ −67.1°; ORD (dioxane), $[\Phi]_{326}^{\text{trough}}$ −5600°, $[\Phi]_{280}^{\text{peak}}$ +6300°, *a*=−119°; MS, *m/e* 344 (M^+); IR, $\nu_{\max}$ 1712, 1211, 1117, 1102, 1032, 974, and 943 cm^{-1}; NMR, δ 1.00 and 1.34 (each 3H, s, 19- and 18-$\mathrm{C\underline{H}_3}$), 3.96 (4H, s, $\mathrm{OC\underline{H}_2C\underline{H}_2O}$), and 5.38 (1H, br W_H= 10 Hz, $\underline{H}$ at C_6). Found: C, 73.22; H, 8.25%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

(ii) A soln of **18** (50 mg) in Py (2 ml) was mixed with a suspended mixture of chromium(VI) oxide (0.5 g) in Py (5 ml), and then stirred at room temp for 5 h. The reaction mixture was filtered through Florisil (3.0 g), which was washed with ether. The filtrate was diluted with water and extracted with ether. The ether soln and ether washings were combined and worked up as usual to give **21** (45 mg), mp 139—142 °C (ether), which was identical with the afore-mentioned sample.

*Reduction of **21** with Sodium Borohydride.* A soln of **21** (330 mg) in methanol (38 ml) was treated with sodium borohydride (660 mg) at room temp for 20 min. The reaction mixture was worked up as usual to give a mixture of alcohols, which was separated into two fractions by chromatography over silica gel (Merck, 10 g). A less-polar fraction eluted with benzene–ether (2 : 1) gave 12α,13α-epoxyetiojerv-5-en-17β-ol-3-one 3-ethylene acetal (**22**, 82 mg), mp 144—146 °C (benzene) and $[\alpha]_D$ −63.1°; MS, *m/e* 346 (M^+) and 328; IR, $\nu_{\max}$ 3480, 1120, 1103, 1033, 1003, and 970 cm^{-1}; NMR, δ 1.00 and 1.38 (each 3H, s, 19- and 18-$\mathrm{C\underline{H}_3}$), 3.94 (4H, s, $\mathrm{OC\underline{H}_2C\underline{H}_2O}$), 4.06 and 5.37 (each 1H, br W_H=7 and 10 Hz, 2$\underline{H}$ at C_{17} and C_6). Found: C, 73.03; H, 8.76%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. A more-polar fraction eluted with benzene–ether (1 : 1 and 1 : 2) gave 17α-alcohol (**18**, 215 mg), mp 159—162 °C (benzene), which was identical with the sample described above.

Compd **22** (45 mg) was treated with Ac_2O (0.5 ml) and Py (1.0 ml) to give 17-acetate (**22a**, 45 mg), mp 144—147 °C (ether) and $[\alpha]_D$ −39.7°; MS, *m/e* 388 (M^+) and 328; IR, $\nu_{\max}$ 1742, 1237, 1098, 1028, 1010, and 968 cm^{-1}; NMR, δ 1.02, 1.26, and 2.09 (each 3H, s, 19- and 18-$\mathrm{C\underline{H}_3}$, and $\mathrm{OCOC\underline{H}_3}$), 3.93 (4H, s, $\mathrm{OC\underline{H}_2C\underline{H}_2O}$), 5.16 and 5.34 (each 1H, br W_H=6 and 10 Hz, 2$\underline{H}$ at C_{17} and C_6). Found: C, 71.33; H, 8.20%. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30%.

*Epoxidation of **17**.* Compd **17** (80 mg) was oxidized with *t*-butyl hydroperoxide (0.05 ml) in the presence of bis(acetylacetonato)oxovanadium(IV) (2 mg) under reflux for 20 min. The reaction mixture was worked up as described before to yield 12β,13β-epoxyetiojerv-5-en-17β-ol-3-one 3-ethylene acetal (**23**, 55 mg), mp 130—132° C (ether) and $[\alpha]_D$ −58.4°; MS, *m/e* 346 (M^+) and 328; IR ($CHCl_3$), $\nu_{\max}$ 3570, 1110, 1062, 1024, 990, and 972 cm^{-1};NMR, δ 1.04 and 1.45 (each 3H, s, 19- and 18-$\mathrm{C\underline{H}_3}$), 3.81 (1H, br W_H=12 Hz, $\underline{H}$ at C_{17}), 3.96 (4H, s, $\mathrm{OC\underline{H}_2C\underline{H}_2O}$), and 5.40 (1H, br W_H=10 Hz, $\underline{H}$ at C_6). Found: C, 72.48; H, 8.75%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

Compd **23** (14 mg) was treated with Ac_2O (0.15 ml) and Py (0.3 ml) to give 17-acetate (**23a**, 11 mg), mp 132—135 °C (ether) and $[\alpha]_D$ −38.0°; MS, *m/e* 388 (M^+), 360, 345, and 328 cm^{-1}; IR ($CHCl_3$), $\nu_{\max}$ 1733, 1245, 1110, 1090, 1025, and 973 cm^{-1}; NMR, δ 1.06, 1.37, and 2.14 (each 3H, s, 19- and 18-$\mathrm{C\underline{H}_3}$, and $\mathrm{OCOC\underline{H}_3}$), 3.98 (4H, s, $\mathrm{OC\underline{H}_2C\underline{H}_2O}$), 5.14 and 5.40 (each 1H, br W_H=12 and 10 Hz, 2$\underline{H}$ at C_{17} and C_6). Found: C, 70.68; H, 7.99%. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30%.

*12β,13β-Epoxyetiojerv-5-ene-3,17-dione 3-Ethylene Acetal (**24**).* Compd **23** (30 mg) in Py (2 ml) was oxidized with chromium (VI) oxide (0.35 g) in Py (3.5 ml) at room temp for 4 h. The reaction mixture was worked up as usual to give an amorphous substance, which was purified by preparative TLC over silica gel (Wakogel B-5, 3 plates) with benzene–ether (2 : 1) to give **24** (24 mg), mp 184—186 °C (ether) and $[\alpha]_D$ −13.4°; ORD (dioxane), $[\Phi]_{280}^{\text{trough}}$ −8500°, $[\Phi]_{324}^{\text{peak}}$ +4000°, a=+125°; MS, *m/e* 344 (M^+); IR ($CHCl_3$), $\nu_{\max}$ 1706, 1230, 1110, 1090, and 1028 cm^{-1}; NMR, δ 1.10 and 1.42 (each 3H, s, 19- and 18-$\mathrm{C\underline{H}_3}$), 3.96 (4H, s, $\mathrm{OC\underline{H}_2C\underline{H}_2O}$), and 5.39 (1H, br W_H=10 Hz, $\underline{H}$ at C_6). Found: C, 72.89; H, 8.45%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.15%.

*Reduction of **24** with Sodium Borohydride.* Compd **24** (18 mg) was treated with sodium borohyride (36 mg) in methanol (4 ml) at room temp for 30 min. The reaction mixture was worked up as described before to give amorphous residue, which was separated into two fractions by preparative TLC over silica gel (Wakogel B-5, 2 plates) with benzene–ether (5 : 1). Less and more polar fractions gave **23** (9 mg), mp 133—135 °C (ether) and **19** (7 mg), mp 136—138 °C (diisopropyl ether), respectively, which were identical with the corresponding authentic sample.

*3β-Hydroxy-12α,13α-epoxyetiojerv-5-en-17-one (**25**).* A soln of **9** (295 mg) in methanol (28 ml) was mixed with 30% aq hydrogen peroxide (1.64 ml) in 4 M aq sodium hydroxide (0.84 ml), and then allowed to stand in a refrigerator (5 °C) for 46 h. The reaction mixture was concentrated, diluted with water, and extracted with chloroform. The chloroform soln was worked up as usual to leave amorphous residue (249 mg), showing a single spot, which on trituration with acetone crystallized, and was then recrystallized from acetone to give **25** (177 mg), mp 173.5—175 °C and $[\alpha]_D$ −92.3°; ORD (dioxane), $[\Phi]_{326}^{\text{trough}}$ −5530°, $[\Phi]_{280}^{\text{peak}}$ +4410°, *a*= −99.4°; MS, *m/e* 302 (M^+), 284, and 269; IR, $\nu_{\max}$ 3480, 1703, and 1062 cm^{-1}; NMR, δ 1.02 and 1.37 (each 3H, s, 19- and 18-$\mathrm{C\underline{H}_3}$), 3.59 and 5.43 (each 1H, br W_H=24 and 10 Hz, 2$\underline{H}$ at C_3 and C_6). Found: C, 75.23; H, 8.61%. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67%.

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