Stereochemistry of the C and D Rings of C-Nor-D-homosteroids. III.[1] The Synthesis of Etiojervane Analogs of Androstan-3β-ol[2]

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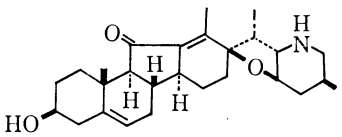
The synthesis of C/D *trans*- and *cis*-fused C-nor-D-homoandrostan-3β-ol 3-acetates (**11a** and **34a**) from jervine (**1**) is described. The configurations of both the compounds and the synthetic intermediates are defined clearly on the basis of the chemical and spectral evidence.

As one of the continuing studies of C-nor-D-homosteroid hormones, we describe herein the transformation of jervine (**1**) into etiojervane analogs of androstan-3β-ol, which include both C/D *cis*- and *trans*-fused ring systems. This synthetic study has also been carried out with an aim to clarify the conformation of C and D rings of etiojervanes on the basis of the NMR and other spectra,[3] and the titled compounds will be useful as reference compounds for a series of these researches.[4,5]

The synthesis of C/D *trans*-fused C-nor-D-homoandrostan-3β-ol (**11**), and its derivatives started from 12β-etiojerv-5-en-3β-ol-11,17-dione 3-acetate[6,7] (**2**), prepared from jervine (**1**) *via* a five-step process. Treatment of **2** with sodium borohydride or with hydrogen over platinum in ethanol effected only reduction of the 17-oxo group to give a 30 : 1 or 2 : 1 mixture[8] of readily separable 17α- and 17β-alcohols (**3a** and **4a**), mp 208.5—209 °C and 173.5—174 °C, in which the hydroxy group at C_{17} was assigned α- and β-configurations, respectively, on the basis of signal patterns of the protons at C_{17}: **3a**, δ 3.08 and W_H=16 Hz; **4a**, δ 3.78 and W_H=6 Hz.[9] In fact, compound **3a** was transformed by the Wolff-Kishner reduction to a known compound, 12β-etiojerv-5-ene-3β,17α-diol[8] (**5**), in good yield. These alcohols, which on acetylation formed the respective 3,17-diacetates (**3b** and **4b**), mp 176—177 °C and 187—188 °C, were reconverted quantitatively into the original ketone (**2**) by oxidation, respectively, confirming the configurational retention at C_{12} and C_{13} during these reactions.



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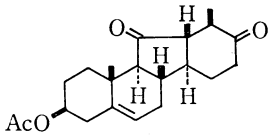

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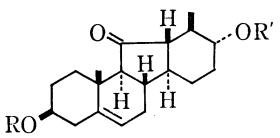
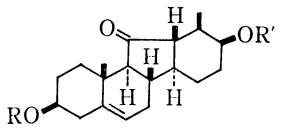
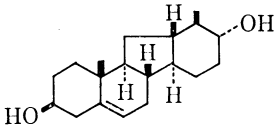


3 R=R′=H
3a R=Ac, R′=H
3b R=R′=Ac
3c R=Ac, R′=Ts



4 R=R′=H
4a R=Ac, R′=H
4b R=R′=Ac



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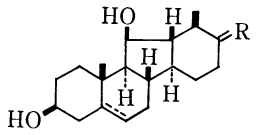
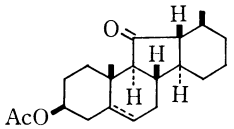
In order to remove the oxygen function at C_{17} and C_{11}, compound **3a** was converted into 17-tosylate (**3c**), mp 106—108 °C, which on treatment with lithium aluminium hydride afforded 3β, 11β-alcohol (**6**), mp 181—183 °C, in good yield. The chemical shift (δ 1.26) of 19-methyl protons in **6** was consistent with the assigned β-configuration to the 11-hydroxy group. Hydrogenation of **6** over platinum in acetic acid gave its 5α,6-dihydro derivative (**7**), mp 148—150 °C, in 83% yield, which was also obtained by the Wolff-Kishner reduction of a well-defined compound **8**,[1] indicative of the retention at C_{12} during the hydride reduction. This glycol **7**, on partial acetylation followed by oxidation with chromic anhydride, produced 11-ketone (**9**), mp 114—114.5 °C, in 70% yield. The transformation of **6** to **9** by the reverse process proceeded in almost the same yield; step 1, partial acetylation of **6** followed by oxidation to Δ^5-11-ketone (**10**), mp 156—157 °C, 69%, and step 2, hydrogenation of **10** to **9**, 76%.

Reduction of 11-ketone **9** by a modification[10] of the Wolff-Kishner reaction produced an aimed compound, 5α,12β-etiojervan-3β-ol (**11**), mp 119—120 °C, in 62% yield, which on acetylation formed 3-acetate (**11a**), mp 72.5—73.5 °C. The β-configuration at C_{12} of this compound (**11**) was determined in an unambiguous manner described below. 5α,12β-Etiojervan-3β-ol-17-one 3-acetate[1] (**12**) with the established configurations at C_{12} and C_{13} was treated with sodium borohydride to give a mixture of 17-alcohols, from which 17α- and 17β-alcohols (**13** and **14**), mp 119—119.5 °C and 96—96.5 °C, were isolated by preparative TLC in 75 and 24% yields, respectively. Treatment of **13** with *p*-toluenesulfonyl chloride followed by reduction with lithium aluminium hydride resulted in formation

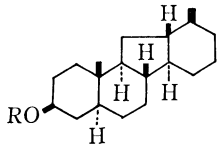
of 3-alcohol, mp 118—119 °C, with a small amount of 3β,17α-glycol[8] (**13a**), mp 166—168 °C. The former was completely identical with compound **11** in all respects.



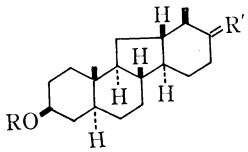
6 Δ^5, R=H_2
7 5αH, R=H_2
8 5αH, R=O



9 5αH
10 Δ^5



11 R=H
11a R=Ac



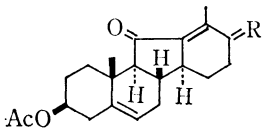
12 R=Ac, R′=O
13 R=Ac, R′=−H, ···OH
13a R=H, R′=−H, ···OH
14 R=Ac, R′=···H, −OH

5α,12α-Etiojervan-3β-ol-11-one 3-acetate (**25**), a 12-epimer of **9**, was synthesized as described below. Treatment of etiojerva-5,12-dien-3β-ol-11,17-dione 3-acetate[6b,7] (**15**) with sodium borohydride in methanol led to only reduction of the 17-oxo group to give a mixture of 17α- and 17β-alcohols (**16** and **17**), mp 170—171 °C and 236—238 °C, which were isolated in 78 and 5% yields, respectively. The configurations at C_{17} of these alcohols were decided on the basis of signal patterns of the protons at C_{17} (**16**, δ 4.20 with W_H of 20 Hz, and **17**, δ 4.06 with W_H of 7 Hz) and optical rotations (**16**, $[\alpha]_D$=−128 °C, and **17**, $[\alpha]_D$=−211°). The assigned configurations were in good accord with the fact that the allylic equatorial proton in cyclohexene systems is more shielded than the corresponding axial,[11] and also with the Mills rule.[12]

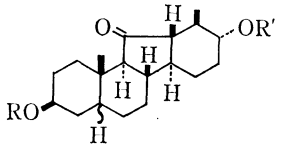
Hydrogenation of compound **16** over Adams platinum in acetic acid produced four stereoisomeric tetrahydro derivatives (**18**—**21**), mp 154—156 °C, 178.5—179 °C, 141—142 °C, and 132—133 °C, in 22, 27, 16, and 25% yields, respectively. The configuration of each product was deduced as described below. Compound **18**, when treated with sodium methoxide in refluxing methanol for 24 h, gave 3,17-alcohol (**18a**), mp 174.5—175 °C, which formed 3,17-diacetate (**18b**), mp 174.5—175 °C. This diacetate (**18b**) was also derived by direct acetylation of monoacetate **18**, indicating that the compound (**18**) was stable under the alkaline conditions. Moreover, glycol **18a** was also obtained by hydrogenation of compound **3** with established configurations in 54% yield. This fact, as coupled with the spectral data (a broad signal at δ 4.65 with W_H of 23 Hz due to the proton at C_3, and a negative Cotton effect with a=−160°,[13]), indicated that compound **18** possessed 5αH, 12βH, 13αH and 17βH configurations. Compound **19** was determined to be a 5-epimer of **18** on the basis of the spectral data: NMR, δ 0.97 (3H, s, 19-C$\underline{H}_3$), 1.27 (3H, d J=6 Hz, 18-C$\underline{H}_3$), and 5.01 (1H, br s W_H=6 Hz, $\underline{H}$ at C_3); ORD, a negative Cotton effect, a=−145°. On the other hand, compound **20** was found to be a 12-epimer of **18** on the following evidence. While compound **20** gave 3,17-diacetate (**20a**), mp 106—109 °C, it was epimerized at C_{12} by treatment with alkali under the same conditions as **18** to give glycol having mp 172—173 °C, quantitatively, which was identical with the afore-mentioned glycol (**18a**) in all respects. These results led to assignment of 5αH, 12αH, 13αH and 17βH configurations to **20**, which was supported by the NMR (19-C$\underline{H}_3$, **20** δ 0.88 and **18** δ 0.84) and ORD spectra (a negative Cotton effect, a=−83°).[13] Finally, the configurations of compound **21** were assigned as shown in the formula (5βH, 12αH, 13αH and 17βH) on the spectral data: NMR, δ 0.88 (3H, d J=7.5 Hz, 18-C$\underline{H}_3$), 1.01 (3H, s, 19-C$\underline{H}_3$), and 5.01 (1H, br s W_H=6 Hz, $\underline{H}$ at C_3); ORD, a negative Cotton effect, a=−77°. As reported previously,[13] hydrogenation of jervine (**1**) under the same conditions as **16** led to formation of C/D *trans*- and *cis*-fused tetrahydro derivatives with α-oriented hydrogens at C_5. The present result was of interest as compared with the hydrogenation result of jervine, because compounds **19** and **21** with β-hydrogens at C_5 were produced in better yields than those **18** and **20** with α-hydrogens at C_5.

5α,12α-Etiojervane-3β,17α-diol-11-one 3-acetate (**20**) was then treated with *p*-toluenesulfonyl chloride in pyridine, and the resulting 17-tosylate (**20b**), amorphous, was refluxed with lithium aluminium hydride in ether to give a single product (**22**), mp 213—214 °C, in 59% yiels from **20**. Contrary to the expectation that the oxygen function at C_{17} would be removed by these reactions, compound **22** had a molecular formula of $C_{19}H_{30}O_2$ and resisted hydrogenation over platinum in acetic acid. The IR spectrum showed the presence of both hydroxy and ether groups at 3405, 1150, 1075, 1060 and 1028 cm^{-1} and the NMR spectrum revealed the existence of three protons on carbon atoms bearing the oxygen functions at δ 3.55 (br W_H=19 Hz, $\underline{H}$ at C_3), 3.90 and 4.31 (each 1H, br s W_H=7 and 5 Hz, 2$\underline{H}$ at C_{17} and C_{11} or *vice versa*). Acetylation of **22** with acetic anhydride in pyridine afforded only monoacetate (**22a**), mp 123—125 °C, which exhibited no hydroxy group in the IR spectrum. All these results indicated this compound to be represented by formula

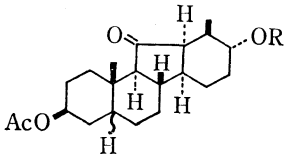
22. Likewise, the 5β-isomer (**21**) was treated in the same manner as **20** to give 17-tosylate (**21a**), mp 120—121 °C, which was submitted to the hydride reduction to yield the corresponding ether compound (**23**), mp 153—154 °C, in moderate yield (crude 89%, pure 24%). Compound **23** also had the same molecular formula, $C_{19}H_{30}O_2$, as **22**, and formed monoacetate (**23a**), mp 128—130 °C, showing the absence of a hydroxy group in the IR spectrum.



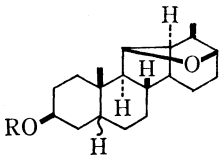
15 R=O
16 R=—H, ···OH
17 R=···H, —OH



18 5αH, R=Ac, R′=H
18a 5αH, R=R′=H
18b 5αH, R=R′=Ac
19 5βH, R=Ac, R′=H



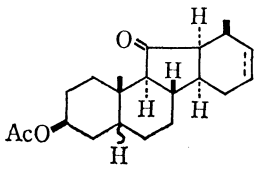
20 5αH, R=H
20a 5αH, R=Ac
20b 5αH, R=Ts
21 5βH, R=H
21a 5βH, R=Ts



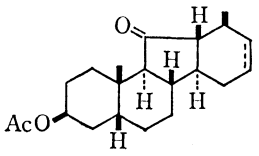
22 5αH, R=H
22a 5αH, R=Ac
23 5βH, R=H
23a 5βH, R=Ac

In order to remove the oxygen function at C_{17}, compound **20** was treated with phosphoryl chloride in pyridine to give olefin (**24**), mp 77—78 °C, in 56% yield, as an only isolable product. The assigned structure with a double bond at C_{16} and C_{17} was deduced from the NMR spectrum; δ 5.84 (2H, t J=5.5 Hz). Hydrogenation of **24** over platinum in acetic acid afforded quantitatively 12α-etiojervan-3β-ol-11-one 3-acetate (**25**), amorphous, which showed a negative Cotton effect of a=—70° in the ORD curve, indicating the configurational retention at C_{12} during the aforementioned reactions. It is to be emphasized that the 19-methyl protons (δ 0.89) of **25** were deshielded 0.04 ppm more than those (δ 0.85) of the corresponding C/D *trans*-fused compound (**9**),[14] and the same difference in chemical shift was observed between the respective 17β-ethyl derivatives.[1] Compound **25**, when treated with alkali in refluxing methanol and then acetylated, gave a quantitative yield of crystalline substance having mp 109—110 °C. This compound was identical with compound **9** in all respects, confirming the 12αH configuration of **25**.

Compound **21** was also treated in the same manner as **20** to give 16,17-olefin (**26**), mp 150—152 °C, in 69% yield, which on hydrogenation produced 5β,12α-etiojervan-3β-ol-11-one 3-acetate (**27**), mp 110—110.5 °C, in 70% yield. Treatment of these 12α-etiojervanes (**26** and **27**) with sodium methoxide in methanol under reflux followed by acetylation effected epimerization at C_{12} to give the corresponding C/D *trans*-fused (12βH) etiojervanes (**28** and **29**), mp 119.5—121 °C and 106—107.5 °C, in quantitative yields, respectively. As expected, the 19-methyl protons of the 12α-epimers (**26** and **27**) were deshielded slightly but definitely (0.02—0.04 ppm) as compared with those of the respective 12β-epimers.



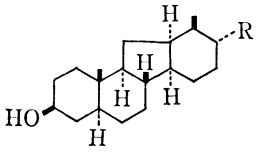
24 5αH, Δ^{16}
25 5αH, no Δ^{16}
26 5βH, Δ^{16}
27 5βH, no Δ^{16}



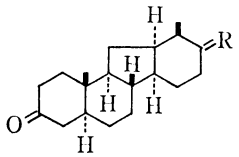
28 Δ^{16}
29 no Δ^{16}

The synthesis of 5α,12α-etiojervan-3β-ol 3-acetate (**34a**), a 12-epimer of compound **11a**, started from 17α-acetyl-5α,12α-etiojervan-3β-ol[4,15] (**30**). The Baeyer-Villiger oxidation of **30** with perbenzoic acid afforded 17-acetate (**31**), amorphous, which on oxidation and subsequent hydrolysis of the resulting 3-ketone (**32**), amorphous, gave 17-hydroxy-3-ketone (**32a**), mp 145—147 °C, in 35% yield from **30**. This compound (**32a**), when oxidized with Jones' reagent, was converted into 3,17-diketone (**33**), mp 173—175 °C, which was identical with the known sample,[16] confirming the 12αH and 13αH configurations of **32a**. This keto-alcohol (**32a**) was transformed smoothly into 17-tosylate (**32b**), amorphous, which on reduction with lithium aluminium hydride in refluxing ether gave rise to the 17-deoxy derivative (**34**), mp 122—124 °C, in 48.5% yield from **32a**. The β-configuration was assigned to the hydroxy group at C_3 on the basis of the NMR spectrum; δ 3.60 (1H, br W_H=20 Hz,

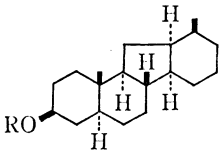
H at C_3). Hence compound **34**, which readily formed 3-acetate (**34a**), mp 97—97.5 °C, was identified as 5α,12α-etiojervan-3β-ol, because the transformation from **30** to **34** involved no epimerization at all asymmetric centers other than C_3. The 19-methyl protons of these C/D *cis*-fused etiojervanes (**34** and **34a**) were observed at lower fields (δ 0.80 and 0.81) than those (δ 0.75 and 0.75) of the corresponding C/D *trans*-fused (**11** and **11a**). These chemical shift differences of 19-methyl protons will be discussed with those of 18-methyl protons in the following paper.[3]



30 R=Ac
31 R=OAc



32 R=−H, ···OAc
32a R=−H, ···OH
32b R=−H, ···OTs
33 R=O



34 R=H
34a R=Ac

Experimental

All the melting points were uncorrected. The homogeneity of each compound was always checked by TLC over silica gel (Wakogel B-5), using various solvent systems, and the spots were developed with ceric sulfate in dil sulfuric acid and/or iodine. The optical rotations, ORD curves and IR spectra were measured in chloroform, dioxane and Nujol, respectively, unless otherwise stated. The NMR spectra were obtained in deuteriochloroform at 60 and/or 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, m, and do" in the NMR spectra denote "singlet, doublet, triplet, quartet, broad, multiplet, and double," respectively.

*12β-Etiojerv-5-ene-3β,17α-diol-11-one (**3**), 12β-Etiojerv-5-ene-3β,17β-diol-11-one (**4**), and Their Derivatives (**3a—3c**, **4a** and **4b**).* a) A solution of 12β-etiojerv-5-en-3β-ol-11,17-dione 3-acetate[6,7] (**2**, 344 mg) in ethanol (32 ml) was hydrogenated over Adams platinum (Pt, 181 mg as $PtO_2 \cdot H_2O$) at room temperature (temp), when 24 ml (1.1 mol) of hydrogen had been consumed for 1 h. The amorphous product (397 mg) showed two main and two minor spots on TLC, the latter two (total 40 mg) being not examined further. The two major components were separated by preparative TLC (16 plates) with a 2 : 3 mixture of ether and benzene. More mobile fractions gave crystalline substance (90 mg), which on recrystallization from acetone-isopropyl ether afforded 17β-alcohol (**4a**, 72 mg), mp 172—173 °C. This was recrystallized twice from the same solvent mixture for analysis: mp 173.5—174 °C; $[\alpha]_D$ −169°; ORD, $[\Phi]_{332}^{trough}$ −10,000°, $[\Phi]_{321}^{trough}$ −6600°, $[\Phi]_{291}^{peak}$ +5800°, $a=-158°$; IR ν_{max} 3590, 1723, 1244, and 1038 cm^{-1}; NMR, δ 1.03 (3H, s, 19-CH_3), 1.29 (3H, d J=5 Hz, 18-CH_3), 2.01 (3H, s, $OCOCH_3$), 3.78 (1H, br s W_H=6 Hz, H at C_{17}), 4.50 (1H, br, H at C_3), and 5.43 (1H, br d J=4 Hz, H at C_6). Found: C, 72.83; H, 8.64%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

Less mobile fractions gave crystalline material (219 mg), which on trituration with acetone-isopropyl ether afforded 17α-alcohol (**3a**, 158 mg), mp 208—209 °C. This was recrystallized twice from the same solvent mixture for analysis: mp 208—209 °C; $[\alpha]_D$ −173.6°; ORD, $[\Phi]_{334}^{trough}$ −12900°, $[\Phi]_{332}^{trough}$ −8800°, $[\Phi]_{292}^{peak}$ +5500°, $a=-184°$; IR, ν_{max} 3340, 1733, 1247, and 1040 cm^{-1}; NMR δ 1.03 (3H, s, 19-CH_3), 1.32 (3H, d J=4 Hz, 18-CH_3), 2.01 (3H, s, $OCOCH_3$), 3.08 (1H, br m W_H=16 Hz, H at C_{17}), 4.56 (1H, br, H at C_3), and 5.39 (1H, br d J=5 Hz, H at C_6). Found: C, 72.74; H, 8.74%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%.

Compound **3a** (54 mg) was treated with acetic anhydride (Ac_2O, 1 ml) and pyridine (Py, 1 ml) at room temp overnight and gave **3b** (50 mg), mp 176—177 °C, on trituration with acetone-isopropyl ether. This was recrystallized from the same solvent mixture for analysis: mp 176—177 °C; $[\alpha]_D$ −168.2°; IR, ν_{max} 1733, 1723, 1649, and 1242 cm^{-1}; NMR, δ 1.04 (3H, s, 19-CH_3), 1.21 (3H, d J=6 Hz, 18-CH_3), 2.02 and 2.04 (each 3H, s, $2OCOCH_3$), 4.49 (2H, br m, 2H at C_3 and C_{17}), and 5.43 (1H, br d J=4 Hz, H at C_6). Found: C, 70.99; H, 8.22%. Calcd for $C_{22}H_{32}O_5$: C, 71.10; H, 8.30%.

Compound **3a** (53 mg) was refluxed with 1 M sodium methoxide in methanol (5.3 ml) for 2 h under a stream of nitrogen. The solvent was evaporated *in vacuo* and the residue was diluted with water and extracted with chloroform, repeatedly. The chloroform solution was washed with water, dried and evaporated to leave crystalline residue (66 mg). The residue showed a single spot on TLC and was triturated with acetone to give **3** (35.5 mg), mp 209—212 °C. Recrystallization from the same solvent afforded an analytical sample, mp 212.5—213 °C; $[\alpha]_D$ −158.2° (MeOH); ORD, $[\Phi]_{333}^{trough}$ −11000°, $[\Phi]_{321}^{trough}$ −7360°, $[\Phi]_{291}^{peak}$ +5700°, $a=-167°$; IR, ν_{max} 3510, 3310, 3230, 1731, and 1044 cm^{-1}. Found: C, 75.00; H, 9.31%. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27%.

Compound **3** (18 mg) was treated with Ac_2O (1 ml) and Py (1 ml) at room temp overnight and gave **3b** (12 mg), mp 175—176 °C, on recrystallization from acetone-isopropyl ether. This sample was identical with the afore-mentioned **3b** (mixed mp, IR and TLC).

A solution of **3a** (708 mg) in Py (10 ml) containing *p*-toluene-sulfonyl chloride (TsCl, 413 mg) was stirred at room temp for 18 h. After further addition of the chloride (534 mg) the whole mixture was allowed to stand at room temp for additional 24 h and poured into ice-water. The resulting precipitates crystallized on trituration with ether-isopropyl ether, had mp 88—90 °C (dec) and amounted to 988 mg. Recrystallization from ether afforded an analytical sample of **3c**, mp 106—108 °C (dec); $[\alpha]_D$ −109.4°; IR, ν_{max} 1733, 1598, 1249, 1190, and 1180 cm^{-1}; NMR, δ 1.03 (3H, s, 19-CH_3), 1.16 (3H, d J=4.5 Hz, 18-CH_3), 2.01 (3H, s, $OCOCH_3$), 2.44 (3H, s, $C_6H_4CH_3$), 4.00 (1H, br, H at

C_{17}), 4.55 (1H, br, H at C_3), and 5.38 (1H, br d J=5 Hz, H at C_6). Found: C, 67.20; H, 7.27, S, 5.78%. Calcd for $C_{28}H_{36}O_6S$: C, 67.18; H, 7.25; S, 6.40%.

Compound **4a** (53 mg) was acetylated in the same manner as mentioned above and afforded **4b** (40 mg), mp 186—187 °C, on trituration with acetone-isopropyl ether. This was recrystallized from the same solvent mixture for analysis: mp 187—188 °C; $[\alpha]_D$ −111.6°; IR, ν_{max} 1734, 1723, 1651, and 1242 cm^{-1}; NMR, δ 1.06 (3H, s, 19-CH_3), 1.20 (3H, d J=5 Hz, 18-CH_3), 2.01 and 2.06 (each 3H, s, 2OCOCH_3), 4.61 (1H, br, H at C_3), 4.99 (1H, br s W_H=6 Hz, H at C_{17}), and 5.44 (1H, br d J=5 Hz, H at C_6). Found C, 71.07; H, 8.32%. Calcd for $C_{22}H_{32}O_5$: C, 71.10; H, 8.30%.

A solution of **4a** (202 mg) was refluxed with 1 M sodium methoxide in methanol (20 ml) for 2 h under nitrogen. After removal of the solvent *in vacuo*, the residue was diluted with water and extracted with chloroform. The chloroform solution was washed with water, dried and evaporated to leave crystalline substance (227 mg), which showed two spots on TLC and crystallized on trituration with acetone-isopropyl ether. This substance (165 mg), mp 168—170 °C, showed a single spot on TLC, and was recrystallized from the same solvent mixture to give an analytical sample of **4**, mp 168—170 °C; ORD, $[\Phi]_{331}^{trough}$ −11060°, $[\Phi]_{319}^{trough}$ −6900°, $[\Phi]_{290}^{peak}$ +6700°, a=−177.6°; IR, ν_{max} 3220 and 1722 cm^{-1}; NMR, δ 1.03 (3H, s, 19-CH_3), 1.33 (3H, br s, 18-CH_3), 3.52 (1H, br, H at C_3), 3.79 (1H, br s W_H=7 Hz, H at C_{17}), and 5.38 (1H, br, H at C_6). Found: C, 75.07; H, 9.42%. Calcd for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27%.

Compound **4** (20 mg) was treated with Ac_2O (1 ml) and Py (1 ml) at room temp overnight and gave its 3,17-diacetate (13 mg), mp 184—185 °C, on trituration with methanol. This compound was identical with the afore-mentioned sample (**4b**) in all respects.

b) To a solution of **2** (1.104 g) in methanol (130 ml) cooled at −7 °C (bath temp) was added sodium borohydride (NBH, 202 mg), and the mixture was stirred at the temp for 1 h. After addition of acetic acid (AcOH, 0.4 ml) the mixture was stirred at room temp for 15 min and concentrated below 30 °C *in vacuo*. The residue was diluted with water and extracted with chloroform repeatedly, and the chloroform solution was washed with 5% aqueous sodium bicarbonate and water, dried and evaporated to leave crystalline residue (1.23 g). Recrystallization from acetone afforded 17α-alcohol (**3a**, 786 mg), mp 206—207 °C, which was identical with the afore-mentioned sample (method a) in all respects.

The filtrate, obtained on recrystallization, was evaporated and separated into three fractions by preparative TLC (10 plates) with a 2 : 3 mixture of ether and benzene. The most mobile part gave amorphous substance (81 mg), which crystallized on trituration with isopropyl ether, had mp 171—173 °C and amounted to 27 mg. This compound was identified as 17β-alcohol (**4a**). Likewise, the middle part (104 mg) afforded **3a** (42 mg), mp 202—204 °C, on trituration with acetone. The least mobile part gave amorphous material (80 mg), which crystallized on trituration with isopropyl ether to give a new 17-alcohol (41 mg), mp 167—171 °C. Recrystallization from acetone-isopropyl ether afforded an analytical sample, mp 173—174 °C; $[\alpha]_D$ −217.1°; ORD, $[\Phi]_{328}^{trough}$ −12400°, $[\Phi]_{317}^{trough}$ −8600°, $[\Phi]_{289}^{peak}$ +5100°, a=−175°; IR, ν_{max} 3520, 1722, 1247, 1038 and 1026 cm^{-1}; NMR, δ 0.83 (3H, d J=7 Hz, 18-CH_3), 1.04 (3H, s, 19-CH_3), 2.02 (3H, s, OCOCH_3), 3.75 (1H, br W_H=16 Hz, H at C_{17}), 4.61 (1H, br, H at C_3), and 5.43 (1H, d J=5 Hz, H at C_6). Found: C, 72.79; H, 8.86%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. The ORD curve and NMR spectrum of this alcohol indicated that this compound would be a 13-epimer of 17α-alcohol (**3a**) and formed from the corresponding 17-ketone included in the starting material as an impurity. This was supported by the spectral data of its 17-acetate described below.

Treatment of the alcohol (50 mg) with Ac_2O (1 ml) and Py (1 ml) at room temp overnight produced its 17-acetate (40 mg), mp 196—198 °C, after trituration with acetone-isopropyl ether. This was recrystallized from the same solvent mixture for analysis: mp 198—199 °C; $[\alpha]_D$ −163.4°; IR, ν_{max} 1734, 1652, 1253, and 1044 cm^{-1}; NMR, δ 0.84 (3H, d J=7 Hz, 18-CH_3), 1.04 (3H, s, 19-CH_3), 2.03 (6H, s, 2OCOCH_3), 4.70 (2H, br m, 2H at C_3 and C_{17}), and 5.43 (1H, br d J=4.5 Hz, H at C_6). Found: C, 71.07; H, 8.42%. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30%.

*Oxidation of **3a** and **4a** to **2**.* Compound **3a** (21 mg) was stirred with a complex prepared from chromic anhydride (CrO_3, 104 mg) and Py (1 ml) at room temp for 14 h. The mixture was diluted with water and extracted with ether, and the ether solution was washed with 1 M hydrochloric acid, 5% aqueous sodium bicarbonate and saturated brine, dried and evaporated to yield amorphous material (24 mg), which crystallized on trituration with isopropyl ether. Recrystallization from the solvent afforded **2** (13 mg), mp 170—171 °C, which was identical with an authentic sample in all respects.

Compound **4a** (25 mg) was treated in the same manner as mentioned above and gave **2** (13 mg), mp 172—173 °C.

*12β-Etiojerv-5-ene-3β,17α-diol (**5**).* To freshly distilled diethylene glycol (DEG, 15 ml) was added sodium (400 mg); the mixture was then heated for a while and cooled. To this solution was added anhydrous hydrazine (6.5 ml), and the mixture was stirred at room temp for a while. After addition of compound **3a** (201 mg), the whole mixture was heated under reflux for 24 h. The excess hydrazine was then removed by distillation and the mixture was again refluxed for additional 17 h. The cooled solution was poured into water (100 ml) and extracted with chloroform. The extracts were washed with 1 M hydrochloric acid, 5% aqueous sodium bicarbonate and water, dried and evaporated to leave oil (446 mg), which was purified by preparative TLC (9 plates) with a 3 : 7 mixture of ethyl acetate and benzene. Main fractions were extracted twice with methanol to give crystalline substance (122.5 mg). This was recrystallized from acetone to afford a pure sample of **5**, mp 180—182 °C, which was identical with an authentic sample[8] in all respects.

*12β-Etiojerv-5-ene-3β,11β-diol (**6**).* 17-Tosylate (**3c**, 921 mg) was treated with lithium aluminium hydride (LAH, 2.0 g) in refluxing tetrahydrofuran (THF, 150 ml) for 18 h under stirring and then cooled with ice-water. After careful addition of water to decompose excess of the hydride, the mixture was submitted to filtration, and the filtrate was evaporated below 30 °C *in vacuo* and then extracted with chloroform. The chloroform solution was worked up as usual to yield amorphous substance (498 mg), which crystallized on trituration with acetone to give **6** (431 mg), mp 180—181 °C. Recrystallization from acetone afforded an analytical sample, mp 181—183 °C; $[\alpha]_D$ −54.5°; IR, ν_{max} 3430 and 1058 cm^{-1}; MNR, δ 1.02 (3H, d J=4 Hz, 18-CH_3), 1.26 (3H, s, 19-CH_3), 3.54 (1H, br, H at C_3), 4.19 (1H, br, m, H at C_{11}), and 5.24 (1H, br s W_H = 9 Hz, H at C_6). Found: C, 78.38; H, 10.25%. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41%.

*5α,12β-Etiojervane-3β,11β-diol (**7**).* a) A solution of **6** (662 mg) in AcOH (30 ml) was hydrogenated over Adams Pt (205 mg) for 30 min, when 57 ml (1.1 mol) of hydrogen had been consumed. The reaction product (870 mg),

obtained on usual work up, crystallized on trituration with isopropyl ether to give **7** (557 mg), mp 148—150 °C, which showed a single spot. Recrystallization from acetone–isopropyl ether afforded an analytical sample, mp 148—150 °C; $[\alpha]_D$ +34.8°; IR, ν_{max} 3380, 1033, and 1024 cm^{-1}; NMR, δ 1.00 (3H, d J=7.5 Hz, 18-C$\underline{H}_3$), 1.03 (3H, s, 19-C$\underline{H}_3$), 3.52 (1H, br, $\underline{H}$ at C_3), and 4.04 (1H, br m, $\underline{H}$ at C_{11}). Found: C, 77.84; H, 11.10%. Calcd for $C_{19}H_{32}O_2$: C, 78.03; H, 11.03%.

b) To a solution of ethylene glycol (10 ml) containing potassium hydroxide (1.1 g) was added 80% hydrazine hydrate (1 ml) and the solution was refluxed for 10 min. To the cooled solution was added compound **8**[1] (74 mg), and the mixture was refluxed for 17 h. After removal of excess of the hydrazine by distillation for 4 h, the reaction mixture was cooled, poured into ice–water (100 ml), and extracted with chloroform. The chloroform extracts gave crystalline substance (90 mg), showing a single spot. Tirturation with acetone–isopropyl ether afforded **7** (55 mg), mp 137—141 °C, which was identical with the afore-mentioned sample (method a).

*5α,12β-Etiojervan-3β-ol-11-one 3-Acetate (**9**).* a) Compound **7** (503 mg) was treated with Ac_2O (2.5 ml) and Py (5 ml) at room temp for 3 h and then poured into ice–water. After being salted out the mixture was extracted with ether, and the ether solution was worked up as usual to yield amorphous residue (655 mg), showing a single spot, which was dissolved in Py (10 ml) and oxidized by careful addition of CrO_3 (1 g) under cooling during 2 min and subsequent stirring at room temp for 12 h. The mixture was dissolved in water (50 ml) under cooling and extracted with ether repeatedly. The ether solution was shaken with 2 M hydrochloric acid to remove the resulting insoluble material by filtration, washed again with 2 M hydrochloric acid, 5% aqueous sodium bicarbonate and saturated brine, dried and evaporated to leave amorphous residue (664 mg), which crystallized on trituration with hexane to give **9** (407 mg), mp 113.5—114 °C. This was recrystallized from hexane for analysis: mp 114—114.5 °C; $[\alpha]_D$ −89.6°; ORD, $[\Phi]^{trough}_{334}$ −9600°, $[\Phi]^{trough}_{323}$ −5400°, $[\Phi]^{peak}_{293}$ +7900°, a=−175°, IR, ν_{max} 1730, 1238, and 1031 cm^{-1}; NMR, δ 0.85 (3H, s, 19-C$\underline{H}_3$), 1.16 (3H, d J=5 Hz, 18-C$\underline{H}_3$), 2.00 (3H, s, OCOC$\underline{H}_3$), and 4.69 (1H, br, $\underline{H}$ at C_3). Found C, 75.74; H, 9.63%. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70%.

b) A solution of compound **10** (382 mg), described later, in AcOH (18 ml) was hydrogenated over Adams Pt (204 mg) at room temp for 1 h, when 25 ml (1.1 mol) of hydrogen had been taken up. The reaction product (405 mg) crystallized on trituration with hexane, had mp 112—113 °C and amounted to 291 mg. Recrystallization from hexane afforded a pure sample of **9**, needles, mp 114—114.5 °C, which was identical with the afore-mentioned sample.

*12β-Etiojerv-5-en-3β-ol-11-one 3-Acetate (**10**).* Compound **6** (411 mg) was treated with Ac_2O (2 ml) and Py (4 ml) at room temp for 3 h, and the resulting crude acetate (517 mg), showing a single spot, was dissolved in Py (6 ml) and poured onto a complex, prepared from CrO_3 (1.05 g) and Py (10 ml), under cooling. The mixture was stirred at room temp for 20 h and, after addition of ethanol (20 ml), evaporated below 30 °C *in vacuo*. The residue was shaken with ether and water, and then filtered to remove insoluble material formed. The ether filtrate gave crystalline residue (516 mg), which was recrystallized from aqueous acetone to yield **10** (364 mg), mp 153—155 °C. Recrystallization from the same solvent afforded an analytical sample, mp 156—157 °C; $[\alpha]_D$ −162.9°; ORD, $[\Phi]^{trough}_{334}$ −12200°, $[\Phi]^{trough}_{322}$ −8300°, $[\Phi]^{peak}_{292}$ +5600°, a=−178°; IR, ν_{max} 1732, 1647, 1248, 1240, and 1043 cm^{-1}; NMR, δ 1.05 (3H, s, 19-C$\underline{H}_3$), 1.19 (3H, d J=5 Hz, 18-C$\underline{H}_3$), 2.01 (3H, s, OCOC$\underline{H}_3$), 4.57 (1H, br, $\underline{H}$ at C_3), and 5.39 (1H, br d J=5 Hz, $\underline{H}$ at C_6). Found: C, 76.46; H, 9.27%. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15%.

*5α,12β-Etiojervan-3β-ol (**11**) and Its 3-Acetate (**11a**).* a) To freshly distilled DEG (15 ml) was dissolved sodium (400 mg) by heating, and to the solution were added anhydrous hydrazine (8 ml) and **9** (193 mg). The solution was refluxed for 22 h and, after removal of the condenser, heated to 230 °C to remove excess of the hydrazine. A new condenser was set up and the solution was again refluxed at the temp for 22 h. After being cooled the solution was poured into water (100 ml) and extracted with chloroform. The chloroform solution gave oily substance, which was purified by preparative TLC (8 plates) with a 3 : 1 mixture of benzene and chloroform. The main fraction was extracted with acetone and, after evaporation, dissolved in chloroform. The chloroform solution was washed with 5% aqueous sodium bicarbonate and water, dried and evaporated to leave crystalline residue (118 mg), which on recrystallization from hexane afforded **11** (89 mg), mp 117.5—118 °C. Further recrystallization from hexane gave an analytical sample, mp 119—120 °C; $[\alpha]_D$ +54.2°; Mass, m/e 276 (M^+) and 258; IR, ν_{max} 3360, 3320, and 1033 cm^{-1}; NMR, δ 0.75 (3H, s, 19-C$\underline{H}_3$), 0.84 (3H, d J=5 Hz, 18-C$\underline{H}_3$), and 3.61 (1H, br, $\underline{H}$ at C_3). Found: C, 82.60; H, 11.72%. Calcd for $C_{19}H_{32}O$: C, 82.54; H, 11.66%.

Acetylation of **11** (62 mg) with Ac_2O (1 ml) and Py (1 ml) at room temp overnight gave **11a** (68 mg), mp 72—72.5 °C, on recrystallization from aqueous methanol. This was recrystallized from the same solvent mixture for analysis: mp 72.5—73.5 °C; $[\alpha]_D$ +40.5°; Mass, m/e 258 (M^+); IR, ν_{max} 1742, 1240, and 1029 cm^{-1}; NMR, δ 0.75 (3H, s, 19-C$\underline{H}_3$), 0.83 (3H, d J=6 Hz, 18-C$\underline{H}_3$), 1.99 (3H, s, OCOC$\underline{H}_3$) and 4.74 (1H, br, $\underline{H}$ at C_3). Found: C, 79.12; H, 10.64%. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76%.

b) Compound **13** (50 mg), described later, was mixed with TsCl (54 mg) in Py (1 ml) under cooling with ice–water and stirring, and the mixture was continuously stirred at room temp for 42 h and then dissolved in chloroform. The chloroform solution, after being worked up as usual, yielded amorphous residue (84 mg), which gave only a single spot and showed absorption maxima at 1722, 1263, and 1174 cm^{-1} in the IR spectrum. This was then dissolved in dry THF (10 ml) and refluxed with LAH (288 mg) for 12 h. After careful addition of water to decompose the hydride, the mixture was extracted with ether repeatedly. The ether solution, on usual work up, gave amorphous residue (68 mg), showing two spots, which was separated by preparative TLC (2 plates) with benzene. The more mobile part (31 mg) crystallized on trituration with hexane to yield **11** (15 mg), mp 118—119 °C, which was identical with the afore-mentioned sample.

The less mobile part (18 mg) gave **13a** (7 mg), mp 166—168 °C, which was identical with an authentic sample of 5α,12β-etiojervane-3β,17α-diol.[8]

*5α,12β-Etiojervane-3β,17α-diol 3-Acetate (**13**) and 5α,12β-Etiojervane-3β,17β-diol 3-Acetate (**14**).* Compound **12**[1] (155 mg) was treated with NBH (74 mg) in methanol (15 ml) at 0 °C for 1 h under stirring. After addition of AcOH (0.2 ml) the mixture was stirred for 10 min, evaporated below 30 °C *in vacuo* and extracted with chloroform repeatedly. The chloroform solution gave amorphous material (173 mg), which was separated into two parts by preparative TLC (7 plates) with a 1 : 3 mixture of ether and benzene. The

more mobile part (38 mg) crystallized on trituration with hexane, had mp 94—94.5 °C and amounted to 10 mg. Recrystallization from hexane afforded an analytical sample of **14**, mp 96—96.5 °C; $[\alpha]_D$ +47.7°; IR, ν_{max} 3535, 3490, 1724, 1239, and 1036 cm^{-1}; NMR δ 0.76 (3H, s, 19-C$\underline{H}_3$), 0.94 (3H, d J=5 Hz, 18-C$\underline{H}_3$), 1.98 (3H, s, OCOC$\underline{H}_3$), 3.78 (1H, br s W_H=5 Hz, $\underline{H}$ at C_{17}), and 4.69 (1H, br, $\underline{H}$ at C_3). Found: C, 75.59; H 10.25%. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25%.

The less mobile part (117 mg) gave **13** (84 mg), mp 119—119.5 °C, on trituration with isopropyl ether. This was recrystallized from isopropyl ether for analysis: mp 119—119.5 °C; $[\alpha]_D$ +26.7°; IR, ν_{max} 3370, 1736, 1241, and 1032 cm^{-1}; NMR, δ 0.76 (3H, s, 19-C$\underline{H}_3$), 0.97 (3H, d J=5 Hz, 18-C$\underline{H}_3$), 1.98 (3H, s, OCOC$\underline{H}_3$), 3.17 (1H, br m W_H=17 Hz, $\underline{H}$ at C_{17}), and 4.68 (1H, br, $\underline{H}$ at C_3). Found: C, 75.68; H, 10.11%. Calcd for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25%.

*Etiojerva-5,12-diene-3β,17α-diol-11-one 3-Acetate (**16**) and Etiojerva-5,12-diene-3β,17β-diol-11-one 3-Acetate (**17**).* To a solution of **15**[6b,7] (2.01 g, mp 180—181 °C) in methanol (200 ml) was added NBH (400 mg) under stirring. After being stirred at room temp for 3 min, the yellow mixture became colorless, and to this mixture was added AcOH (1.5 ml) to decompose excess of the hydride. After being kept at room temp for 10 min, the mixture was concentrated below 35 °C *in vacuo*, and the resulting residue was diluted with water (100 ml) and extracted with chloroform. The chloroform solution, after being worked up as usual, left crystalline residue (2.05 g), which was separated into two parts by preparative TLC (43 plates) with a 1 : 2 mixture of ether and benzene. The more mobile part (143 mg) crystallized on trituration with acetone, had mp 236—237 °C and amounted to 133 mg. Recrystallization from acetone-isopropyl ether afforded an analytical sample of **17**, mp 236—238 °C; $[\alpha]_D$ −211.0°; IR, ν_{max} 3535, 1726, 1703, 1633, 1239, 1231, and 1041 cm^{-1}; NMR, δ 1.05 (3H, s, 19-C$\underline{H}_3$), 2.00 (3H, s, OCOC$\underline{H}_3$), 2.23 (3H, s, 18-C$\underline{H}_3$), 4.06 (1H, br s W_H=7 Hz, $\underline{H}$ at C_{17}), 4.58 (1H, br W_H=18 Hz, $\underline{H}$ at C_3), and 5.38 (1H, br s W_H=9 Hz, $\underline{H}$ at C_6). Found: C, 73.33; H, 8.23%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

The less mobile part (1.837 g) gave **16** (1.622 g), mp 170—171 °C, on trituration with acetone-isopropyl ether. This was recrystallized from the same solvent mixture for analysis: mp 170—171 °C; $[\alpha]_D$ −128.0°; IR, ν_{max} 3320, 1738, 1710, 1639, 1243, and 1045 cm^{-1}; NMR, δ 1.06 (3H, s, 19-C$\underline{H}_3$), 2.00 (3H, s, OCOC$\underline{H}_3$), 2.18 (3H, s, 18-C$\underline{H}_3$), 4.20 (1H, br W_H=20 Hz, $\underline{H}$ at C_{17}) 4.57 (1H, br W_H=20.5 Hz $\underline{H}$ at C_3), and 5.38 (1H, br s W_H=8.5 Hz, $\underline{H}$ at C_6). Found: C, 73.24; H, 8.26%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

*Hydrogenation of **16**.* A solution of **16** (1.401 g) in AcOH (50 ml) was hydrogenated over Adams Pt (504 mg) in AcOH (10 ml) at room temp for 10 h, when 2.2 mol of hydrogen had been consumed. The reaction product (1.613 g), after being worked up as usual, showed four spots on TLC and was separated by preparative TLC (77 plates) with a 1 : 1 mixture of ether and benzene. The most mobile fraction, extracted with acetone, gave crystalline substance (306 mg), which on recrystallization from acetone-isopropyl ether afforded 5α,12β-etiojervane-3β,17α-diol-11-one 3-acetate (**18**, 155 mg), mp 154—156 °C. This was recrystallized from the same solvent mixture for analysis: mp 155—156 °C; $[\alpha]_D$ −74.6°; ORD, $[\Phi]_{333}^{trough}$ −8200°, $[\Phi]_{323}^{trough}$ −4500°, $[\Phi]_{292}^{peak}$ +7800°, a=−160°; IR, ν_{max} 3375, 1732, 1244, and 1034 cm^{-1}; NMR, δ 0.84 (3H, s, 19-C$\underline{H}_3$), 1.27 (3H, d J=5.5 Hz, 18-C$\underline{H}_3$), 1.98 (3H, s, OCOC$\underline{H}_3$), 3.11 (1H, br W_H=20.5 Hz, $\underline{H}$ at C_{17}), and 4.65 (1H, br W_H=23 Hz, $\underline{H}$ at C_3). Found: C, 72.27; H, 9.18%. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26%.

The second mobile fraction gave crystalline substance (390 mg), which on recrystallization from acetone-isopropyl ether afforded 5β,12β-etiojervane-3β,17α-diol-11-one 3-acetate (**19**, 312 mg), mp 177—178 °C. This was recrystallized from the same solvent mixture for analysis: mp 178.5—179 °C; $[\alpha]_D$ −80.6°; ORD, $[\Phi]_{331}^{trough}$ −7500°, $[\Phi]_{322}^{trough}$ −4700°, $[\Phi]_{289}^{peak}$ +6900°, a=−144°; IR, ν_{max} 3505, 1723, 1229, and 1045 cm^{-1}; NMR, δ 0.97 (3H, s, 19-C$\underline{H}_3$), 1.27 (3H, d J=6 Hz, 18-C$\underline{H}_3$), 2.01 (3H, s, OCOC$\underline{H}_3$), 3.06 (1H, br W_H=20.6 Hz, $\underline{H}$ at C_{17}), and 5.01 (1H, br s W_H=6 Hz, $\underline{H}$ at C_3). Found: C, 72.09; H, 9.26%. Calcd for $C_{21}H_{32}O_4$: C, 72.38, H, 9.26%.

The third fraction gave crystalline material (317 mg), which afforded 5α,12α-etiojervane-3β,17α-diol-11-one 3-acetate (**20**, 152 mg), mp 139.5—140.5 °C, on trituration with acetone-isopropyl ether. This was recrystallized from the same solvent mixture for analysis: mp 141—142 °C; $[\alpha]_D$ −10.1°; ORD, $[\Phi]_{331}^{trough}$ −3500°, $[\Phi]_{290}^{peak}$ +4800°, a=−83°; IR, ν_{max} 3505, 1729, 1240, and 1031 cm^{-1}; NMR, δ 0.88 (3H, s, 19-C$\underline{H}_3$), 0.89 (3H, d J=7 Hz, 18-C$\underline{H}_3$), 1.98 (3H, s, OCOC$\underline{H}_3$), 3.81 (1H, br s W_H=9 Hz, $\underline{H}$ at C_{17}), and 4.67 (1H, br W_H=20 Hz, $\underline{H}$ at C_3). Found: C, 72.77; H, 9.47%. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26%.

Compound **20** (18 mg) was acetylated with Ac_2O (0.2 ml) and Py (0.2 ml) at room temp for 38 h, and gave crystalline substance (21 mg), which showed a single spot on TLC and yielded **20a**, mp 106—109 °C, on trituration with isopropyl ether: NMR, δ 0.88 (3H, s, 19-C$\underline{H}_3$), 0.92 (3H, d J=7 Hz, 18-C$\underline{H}_3$), 2.00 (6H, s 2OCOC$\underline{H}_3$), 4.68 (1H, br W_H=26 Hz, $\underline{H}$ at C_3), and 4.80 (1H, br s W_H=10.5 Hz, $\underline{H}$ at C_{17}).

The least mobile fraction (393 mg) was triturated with acetone-isopropyl ether to give 5β,12α-etiojervane-3β-17α-diol-11-one 3-acetate (**21**, 237 mg), mp 130—132 °C. Recrystallization from the same solvent mixture afforded an analytical sample, mp 132—133 °C; $[\alpha]_D$ −17.4°; ORD, $[\Phi]_{330}^{trough}$ −3900°, $[\Phi]_{290}^{peak}$ +3800°, a=−77°; IR, ν_{max} 3530, 1731, 1240, and 1024 cm^{-1}; NMR, δ 0.88 (3H, d J=7.5 Hz, 18-C$\underline{H}_3$), 1.01 (3H, s, 19-C$\underline{H}_3$), 2.01 (3H, s, OCOC$\underline{H}_3$), 3.80 (1H, br s W_H=9.5 Hz, $\underline{H}$ at C_{17}), and (1H, br s W_H=6 Hz, $\underline{H}$ at C_3). Found: C, 72.46; H, 9.26%. Calcd for $C_{21}H_{32}O_4$: C, 72.38; H, 9.26%.

*5α,12β-Etiojervane-3β,17α-diol-11-one (**18a**) and Its 3,17-Diacetate (**18b**).* a) Compound **3** (95 mg) was dissolved in AcOH (6 ml) and hydrogenated over Adams Pt (60 mg) at room temp, when 1 mol of hydrogen had been taken up for 1 h. The resulting amorphous product (112 mg) was purified by preparative TLC (4 plates) with ether to give amorphous substance (84 mg), which on trituration with acetone-isopropyl ether crystallized, had mp 168—170 °C and amounted to 46 mg. This was recrystallized from the same solvent mixture to give **18a** in pure state, mp 175—176 °C; $[\alpha]_D$ −66.6°; IR, ν_{max} 3420, 1725, and 1029 cm^{-1}; NMR, δ 0.83 (3H, s, 19-C$\underline{H}_3$), 1.29 (3H, d J=5 Hz, 18-C$\underline{H}_3$), 3.07 (1H, br W_H=18 Hz, $\underline{H}$ at C_{17}), and 3.60 (1H, br W_H=22 Hz, $\underline{H}$ at C_3). Found: C, 73.33; H, 10.02%. Calcd for $C_{19}H_{30}O_3 \cdot 0.5CH_3COCH_3$: C, 73.39; H, 9.92%.

Compound **18a** (32 mg) was treated with Ac_2O (0.2 ml) and Py (0.2 ml) at room temp overnight and gave **18b** (33 mg), mp 226—226.5 °C, on trituration with acetone-isopropyl ether. This was recrystallized from the same solvent mixture for analysis: mp 226—226.5 °C; IR, ν_{max} 1731, 1244, and 1025 cm^{-1}; NMR, δ 0.86 (3H, s, 19-C$\underline{H}_3$), 1.18 (3H, d

J=6 Hz, 18-CH_3), 1.99 and 2.02 (each 3H, s 2OCOCH_3), and 5.50 (2H, br m, 2H at C_3 and C_7). Found: C, 70.98; H, 8.78%. Calcd for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78%.

b) A solution of **18** (50 mg) in methanol (10 ml) was refluxed with 1 M sodium methoxide under a stream of nitrogen. Ths solution was concentrated *in vacuo* and the resulting residue was diluted with water and then extracted with chloroform. The chloroform solution was washed with water, dried and evaporated to leave amorphous substance (60 mg), which showed a single spot on TLC and gave diol (36 mg), mp 174.5—175 °C, on trituration with acetone–isopropyl ether. This compound was identical with the afore-mentioned sample of **18a**.

Compound **18** (30 mg) was also treated with Ac_2O (0.5 ml) and Py (0.5 ml) at room temp overnight and gave its 17-acetyl derivative (32 mg), mp 225.5—226 °C, on trituration with acetone–isopropyl ether. This was identical with an authentic sample of **18b**, described in the section a.

c) A solution of compound **20** (22 mg) in methanol (10 ml) was refluxed with 1 M sodium methoxide under a stream of nitrogen for 24 h. The solution was worked up as usual to leave foamy residue (26.5 mg). This showed a single spot on TLC and was triturated with acetone–isopropyl ether to give crystalline substance (12 mg), mp 172—173 °C, which was identical with an authentic sample of **18a** in all respects.

*11β,17β-Oxido-5α,12α-etiojervan-3β-ol (**22**) and Its 3-Acetate (**22a**).* A solution of **20** (40 mg) in Py (1 ml) containing TsCl (102 mg) was stirred at room temp for 40 h and poured into ice–water, and then extracted with chloroform repeatedly. The chloroform solution was washed with 1 M hydrochloric acid, 5% aqueous sodium bicarbonate and water, dried and evaporated below 30 °C to leave 17-tosylate (**20b**, 56.5 mg), amorphous, which showed a single spot on TLC; IR ($CHCl_3$), ν_{max} 1730, 1600, 1492, 1253, 1177, and 1027 cm^{-1}; NMR, δ 0.79 (3H, d J=6 Hz, 18-CH_3), 0.87 (3H, s, 19-CH_3), 1.98 (3H, s, OCOCH_3), 2.42 (3H, s, $C_6H_4CH_3$), 4.55 (2H, br W_H=15 Hz, 2H at C_3 and C_{17}), and 7.30 and 7.75 (each 2H, d J=8 Hz, $C_6H_4CH_3$).

Tosylate **20b** (56.5 mg) was treated with LAH (170 mg) in refluxing ether (15 ml) for 5 h under stirring and then cooled with ice–water. After careful addition of water, the mixture was extracted with ether repeatedly. The ether solution gave crystalline material (41.5 mg), which showed practically a single spot and was purified by preparative TLC (2 plates) with a 2 : 1 mixture of ether and benzene. The main fraction, extracted with acetone, gave crystalline substance (19.5 mg), which on recrystallization from isopropyl ether afforded **22** (13 mg), mp 207—208 °C. Recrystallization from acetone–isopropyl ether yielded an analytical sample, mp 213—214 °C; $[\alpha]_D$ −18.5 °; IR, ν_{max} 3405, 1150, 1075, 1060, and 1028 cm^{-1}; NMR, δ 0.95 (3H, d J=6 Hz, 18-CH_3), 0.98 (3H, s, 19-CH_3), 3.55 (1H, br W_H=19 Hz, H at C_3), 3.90 and 4.31 (each 1H, br s W_H=7 and 5 Hz, 2H at C_{11} and C_{17} or *vice versa*). Found: C, 78.73; H, 10.42%. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41%.

Compound **22** (15 mg) was acetylated with Ac_2O (0.4 ml) and Py (0.4 ml) at room temp overnight to give **22a** (9 mg), mp 123—125 °C, on trituration with aqueous methanol: Mass, *m/e* 332 (M^+); IR, ν_{max} 1741, 1246, 1146, 1060, 1023, and 1005 cm^{-1}; NMR, δ 0.94 (3H, d J=6 Hz, 18-CH_3), 0.99 (3H, s, 19-CH_3), 1.99 (3H, s, OCOCH_3), 3.92 and 4.31 (each 1H, br s W_H=7 and 6 Hz, 2H at C_{11} and C_{17} or *vice versa*), and 4.68 (1H, br W_H=26 Hz, H at C_3).

*11β,17β-Oxide-5β,12α-etiojervan-3β-ol (**23**) and Its 3-Acetate (**23a**).* A solution of **21** (103 mg) in Py (1.5 ml) containing TsCl (204 mg) was stirred at room temp for 40 h and poured into ice–water and then extracted with chloroform repeatedly. The chloroform solution gave crystalline substance (185 mg), which showed a single spot and afforded 17-tosylate (**21a**, 130 mg) mp 120—121 °C, on trituration with isopropyl ether: IR, ν_{max} 1732, 1602, 1351, 1245, 1188, 1177, 1030, 1021, 840, and 819 cm^{-1}; NMR, δ 0.80 (3H, d J=7.5 Hz, 18-CH_3), 0.99 (3H, s, 19-CH_3), 2.03 (3H, s, OCOCH_3), 2.44 (3H, s, $C_6H_4CH_3$), 4.59 (1H, br s W_H=8.5 Hz, H at C_{17}), 5.04 (1H, br s W_H=7 Hz, H at C_3), and 2.65 and 2.21 (each 2H, d J=8 Hz, $C_6H_4CH_3$).

Tosylate **21a** (129 mg) was treated with LAH (238 mg) in refluxing ether (10 ml) for 4 h under stirring and then cooled with ice–water. After careful decomposition of excess of the hydride with water, the mixture was extracted with ether repeatedly. The ether solution gave crystalline substance (74 mg), which showed a single spot and afforded **23** (20 mg), mp 153—154 °C, on trituration with isopropyl ether: IR ($CHCl_3$), ν_{max} 3600, 3390, 1146, 1090, and 1003 cm^{-1}; NMR, δ 0.95 (3H, d J=7 Hz, 18-CH_3), 1.10 (3H, s, 19-CH_3), and 3.92, 4.04 and 4.30 (each 1H, br s W_H=8, 6 and 5 Hz, 3H at C_{11}, C_3 and C_{17} cr *vice versa*).

Compound **23** (75 mg) was acetylated with Ac_2O (1 ml) in Py (1 ml) at room temp overnight and gave **23a** (70 mg), mp 121—123 °C, on trituration with aqueous methanol. Recrystallization from the same solvent mixture afforded an analytical sample, mp 128—130 °C; $[\alpha]_D$ −11.0°; Mass, *m/e* 332 (M^+); IR, ν_{max} 1741, 1247, 1096, and 1027 cm^{-1}; NMR, δ 0.96 (3H, d J=6.5 Hz, 18-CH_3), 1.11 (3H, s, 19-CH_3), 2.01 (3H, s, OCOCH_3), and 3.91, 4.33 and 5.04 (each 1H, br s W_H=7, 6 and 6 Hz, 3H at C_{11}, C_{17} and C_3 or *vice versa*). Found: C, 75.95; H, 9.66%. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70%.

*5α,12α-Etiojerv-16-en-3β-ol-11-one 3-Acetate (**24**).* A solution of **20** (77 mg) in dry Py (1.5 ml) was treated with phosphoryl chloride (0.3 ml) at room temp for 15.5 h. The mixture was poured into crushed ice and extracted with chloroform. The chloroform solution gave oily substance (61 mg), which was purified by preparative TLC with a 1 : 10 mixture of ether and benzene. The resulting oily residue (41 mg) was triturated into aqueous methanol to yield **24** (19 mg), mp 77—78 °C; $[\alpha]_D$ +53.7°; IR, ν_{max} 3010 (sh), 1735, 1722 (sh), 1640, 1240, 1027, and 695 cm^{-1}; NMR, δ 0.87 (3H, s, 19-CH_3), 0.92 (3H, d J=6.5 Hz, 18-CH_3), 2.00 (3H, s, OCOCH_3), 4.66 (1H, br W_H= 31 Hz, H at C_3), and 5.84 (2H, t J=5.5 Hz, 2H at C_{16} and C_{17}).

*5α,12α-Etiojervan-3β-ol-11-one 3-Acetate (**25**).* Compound **24** (53 mg) was hydrogenated over Adams Pt (31 mg) in AcOH (3 ml) at room temp for 30 min, when 1.2 mol of hydrogen had been consumed. The catalyst was removed by filtration and the filtrate was concentrated below 30 °C under reduced pressure and dissolved in chloroform. The chloroform solution was worked up at usual to give **25** (50 mg), amorphous, which resisted crystallization: $[\alpha]_D$ −11.1°; ORD, $[\Phi]_{333}^{trough}$ −3010°, $[\Phi]_{316}$ 0°, $[\Phi]_{290}^{peak}$ +3980°, a= −69.9°; Mass, *m/e* 332 (M^+); IR ($CHCl_3$), ν_{max} 1728 and 1245 cm^{-1}; NMR, δ 0.90 (3H, s, 19-CH_3), 0.92 (3H, d J= 6 Hz, 18-CH_3), 2.02 (3H, s, OCOCH_3), and 4.67 (1H, br W_H=24 Hz, H at C_3).

*Epimerization of **25** to **9**.* A solution of compound **25** (33 mg) in methanol (15 ml) containing 5% potassium hydroxide was refluxed under nitrogen for 2 h. The solution was evaporated, diluted with water and extracted with chloroform. The extracts were washed with water, dried and evaporated to leave amorphous residue (27.4 mg), which was acetylated with Ac_2O (0.5 ml) in Py (0.5 ml) at room temp overnight. After usual work up, the amorphous

reaction mixture (31 mg) crystallized on trituration with aqueous methanol to give crystalline substance (7 mg) having mp 108.5—110 °C, which was identical with an authentic sample of **9** in all respects.

*5β,12α-Etiojerv-16-en-3β-ol-11-one 3-Acetate (**26**).* A solution of compound **21** (144 mg) in dry Py (2.5 ml) was treated with phosphoryl chloride (0.5 ml) at room temp for 14 h. The mixture was worked up in the same manner as the corresponding 5α-mixture to leave oily residue (141 mg), which was purified by preparative TLC (9 plates) with a 1 : 10 mixture of ether and benzene. The main fraction was extracted with acetone and afforded crystalline residue (94 mg), which on trituration with aqueous methanol yielded **26** (63 mg), mp 146—152 °C. Recrystallization from the same solvent mixture gave an analytical sample, mp 150—152 °C; $[\alpha]_D$ +47.4°; IR, ν_{max} 3010, 1729, 1640, 1240, 1023, and 699 cm^{-1}; NMR, δ 0.92 (3H, d J=7 Hz, 18-C$\underline{H}_3$), 1.02 (3H, s, 19-C$\underline{H}_3$), 2.03 (3H, s, OCOC$\underline{H}_3$), 5.04 (1H, br s W_H=7.5 Hz, $\underline{H}$ at C_3), and 5.86 (2H, t J= 6 Hz, 2$\underline{H}$ at C_{16} and C_{17}). Found: C, 76.13; H, 9.18%. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15%.

*Epimerization of **26** to **28**.* Compound **26** (32 mg) in methanol (12 ml) was treated with 1 M sodium methoxide under reflux for 17 h. After evaporation of the solvent, the mixture was diluted with water and extracted with chloroform. The chloroform solution left crystalline substance (25.5 mg), showing a single spot on TLC, which was acetylated with Ac_2O (0.4 ml) and Py (0.4 ml) at room temp overnight to give crystalline material (30 mg). This was triturated with aqueous methanol to give **28** (20 mg), mp 119.5—121 °C; NMR, δ 1.00 (3H, s, 19-C$\underline{H}_3$), 1.30 (3H, d J= 6 Hz, 18-C$\underline{H}_3$), 2.04 (3H, s, OCOC$\underline{H}_3$), 5.04 (1H, br s W_H=7 Hz, $\underline{H}$ at C_3), and 5.49 (2H, br s W_H=10 Hz, 2$\underline{H}$ at C_{16} and C_{17}).

*5β,12α-Etiojervan-3β-ol-11-one 3-Acetate (**27**).* A solution of compound **26** (50 mg) in AcOH (1 ml) was hydrogenated over Adams Pt (30 mg) at room temp for 2 h, when 1.2 mol of hydrogen had been consumed. The reaction mixture, after being worked up as usual, gave amorphous substance (54 mg), which showed a single spot on TLC and was triturated with aqueous methanol to yield **27** (35 mg), mp 106—109 °C. Recrystallization from the same solvent mixture gave an analytical sample, mp 110—110.5 °C; $[\alpha]_D$ −15.9 °; IR, ν_{max} 1727, 1250, 1240, and 1029 cm^{-1}; NMR, δ 0.91 (3H, d J=7.5 Hz, 18-C$\underline{H}_3$), 1.03 (3H, s, 19-C$\underline{H}_3$), 2.02 (3H, s, OCOC$\underline{H}_3$), and 5.02 (1H, br s W_H= 8 Hz, $\underline{H}$ at C_3). Found: C, 75.77; H, 9.59;% Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70%.

*Epimerization of **27** to **29**.* Compound **27** (39 mg) in methanol (17 ml) was treated with 1 M sodium methoxide under reflux for 17 h. After being worked up as usual, the mixture gave crystalline substance (29.5 mg), which was acetylated with Ac_2O (0.4 ml) and Py (0.4 ml) at room temp overnight. The resulting amorphous acetate crystallized on trituration with aqueous methanol to yield **29** (20 mg), mp 106—107.5 °C; IR, ν_{max} 1743, 1725, 1237, 1028, and 1017 cm^{-1}; NMR, δ 1.00 (3H, s, 19-C$\underline{H}_3$), 1.17 (3H, d J=5 Hz, 18-C$\underline{H}_3$), 2.03 (3H, s, OCOC$\underline{H}_3$), and 5.02 (1H, br s W_H=6 Hz, $\underline{H}$ at C_3).

*5α,12α-Etiojervan-17α-ol-3-one (**32a**).* To compound **30** (809 mg) in chloroform (10 ml) was added a chloroform solution (10 ml) containing perbenzoic acid (activity 83.3%, 611 mg) at 0 °C, and the mixture was allowed to stand at room temp for 86 h. The perbenzoic acid solution (10 ml) was again added to the mixture, and the whole solution was kept at room temp for additional 71 h. The solution was washed with 0.1 M aqueous sodium thiosulfate (4×20 ml), 5% aqueous sodium bicarbonate (2×10 ml) and water (2×20 ml), dried and evaporated to leave amorphous residue (**31**, 863 mg), which showed almost a single spot on TLC; IR ($CHCl_3$), ν_{max} 3620, 3460, 1720, 1252, and 1029 cm^{-1}.

To a cooled solution of the whole residue in acetone (20 ml) was added Jones' reagent (1 ml) under stirring, and the mixture was stirred at 0 °C for 50 min. After addition of ethanol (1.2 ml) the mixture was stirred for another 15 min and concentrated *in vacuo*. The residue was worked up as usual to give resinous substance (802 mg), which without purification was refluxed in a methanol solution (16 ml) containing 5% potassium hydroxide under nitrogen for 1 h. The resulting amorphous product (614 mg) showed two spots and was separated by preparative TLC (25 plates) with a 1 : 3 mixture of ether and benzene. More mobile fractions gave oily substance (204 mg), which on trituration with a mixture of acetone and isopropyl ether afforded crystalline substance, mp 82.5—84 °C, which would probably be the unreacted starting material: Mass, *m/e* 316 (M^+); NMR, δ 0.80 (3H, d J=6 Hz, 18-C$\underline{H}_3$), 0.99 (3H, s, 19-C$\underline{H}_3$), and 2.16 (3H, s, 21-C$\underline{H}_3$). Less mobile fractions gave crystalline material (318 mg), which on recrystallization from acetone-isopropyl ether afforded **32a** (248 mg), mp 143—145 °C. This was recrystallized from the same solvent mixture for analysis: mp 145—146.5 °C; $[\alpha]_D$ −5.5°; Mass, *m/e* 290 (M^+); IR, ν_{max} 3497, 1708, 1065, and 1036 cm^{-1}; NMR, δ 0.96 (3H, s, 19-C$\underline{H}_3$), 1.00 (3H, d J=6 Hz, 18-C$\underline{H}_3$), and 3.45 (1H, do t J=10, 10 and 4 Hz, $\underline{H}$ at C_{17}). Found: C, 78.40; H, 10.32%. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41%.

*5α,12α-Etiojervane-3,17-dione (**33**).* To a cold solution of compound **32a** (50 mg) in acetone (2 ml) was added Jones' reagent (0.2 ml) under stirring, and the mixture was stirred at 0 °C for 70 min. After addition of ethanol (0.3 ml), the mixture was concentrated *in vacuo*, and the residue was diluted with water and then extracted with chloroform. The chloroform solution was worked up as usual to yield oily substance (54 mg), which on trituration with acetone gave **33** (27 mg), mp 160—162 °C. This was recrystallized twice from ether to give a pure sample, mp 173—175 °C, which was identical with an authentic sample, prepared by the procedure of Johns and Laos (lit,[16] mp 169—170 °C).

*5α,12α-Etiojervan-3β-ol (**34**) and Its 3-Acetate (**34a**).* To a cold solution of compound **32a** (100 mg) in Py (2 ml) was added TsCl (100 mg), and the mixture was stirred at room temp for 48 h, diluted with water and extracted with chloroform. The chloroform solution gave oily substance (146 mg); IR ($CHCl_3$), ν_{max} 1707, 1601, 1176, 918, and 894 cm^{-1}.

The oily substance was dissolved in dry ether (20 ml) and refluxed with LAH (300 mg) under stirring for 13 h. After careful decomposition of excess of the hydride with water, the resulting heterogeneous mixture was shaken with 1 M hydrochloric acid and extracted with ether. The ether extracts left amorphous residue (97 mg), showing a single spot on TLC, which was triturated with acetone to give **34** (46 mg), mp 121—123 °C. This was recrystallized twice from aqueous acetone for analysis: mp 129.5—130 °C; $[\alpha]_D$ −31.0°; Mass, *m/e* 276 (M^+), 258, and 243; IR, ν_{max} 3380, 1045, and 1030 cm^{-1}; NMR, δ 0.79 (3H, s, 19-C$\underline{H}_3$), 0.79 (3H, d J=6 Hz, 18-C$\underline{H}_3$), and 3.58 (1H, br W_H= 22 Hz, $\underline{H}$ at C_3). Found: C, 82.68; H, 11.28%. Calcd for $C_{19}H_{32}O$: C, 82.54; H, 11.66%.

Compound **34** (42 mg) was acetylated with Ac_2O (1 ml) and Py (1 ml) at room temp overnight and gave oily substance (46 mg), which on trituration with methanol crystallized to yield **34a** (32 mg), mp 95.5—96 °C. This was recrystallized from the same solvent to give an analytical

sample, mp 97—97.5 °C; $[\alpha]_D$ −47.4°; Mass, *m/e* 258 (M^+); IR, ν_{max} 1738, 1234, and 1022 cm^{-1}; NMR, δ 0.80 (3H, d J=6 Hz, 18-CH_3), 0.81 (3H, s, 19-CH_3), 2.00 (3H, s, $OCOCH_3$), and 4.71 (1H, br W_H=27 Hz, H at C_3). Found: C, 79.23; H, 10.52%. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76%.

References

1) Part II, A Murai, T. Nishimura, and T. Masamune, *Bull. Chem. Soc. Jpn.*, **49**, 1602 (1976).

2) Part XXIV of "C-Nor-D-homosteroids and Related Alkaloids"; Part XXIII, Ref. 1.

3) T. Masamune, A. Murai, K. Nishizakura, T. Orito, S. Numata, and H. Sasamori, *Bull. Chem. Soc. Jpn.*, **49**, 1622 (1976).

4) A. Murai, K. Arita, and T. Masamune, *Bull. Chem. Soc. Jpn*, **46**, 3536 (1973).

5) T. Masamune, N. Sato, K. Kobayashi, I. Yamazaki, and Y. Mori, *Tetrahedron*, **23**, 1591 (1967).

6) a) T. Masamune, A. Murai, and S. Numata, *Tetrahedron.*, **25**, 3145 (1969). b) S. M. Kupchan and S. D. Levine, *J. Am. Chem. Soc.*, **86**, 701 (1964).

7) J. Fried and A. Klingsberg, *J. Am. Chem. Soc.*, **75**, 4929 (1953).

8) T. Masamune and K. Orito, *Tetrahedron*, **25**, 4551 (1969).

9) N. S. Bhacca and D. H. Williams, "Application of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco (1964), p. 79.

10) D. H. R. Barton, D. A. J. Ives, and B. R. Thomas, *J. Chem. Soc.*, **1955**, 2056.

11) The allylic equatorial proton of cyclohexene system is more shielded than the corresponding axial proton; G. F. H. Green, J. E. Page, and S. E. Staniforth, *J. Chem. Soc., B*, **1966**, 807.

12) J. A. Mills, *J. Chem. Soc.*, **1952**, 4976; A. K. Bose and G. Chatterjee, *J. Org. Chem.*, **23**, 1425 (1958); R. K. Hill and J. W. Morgan, *ibid.*, **33**, 927 (1968); J. H. Brewster, *J. Am. Chem. Soc.*, **81**, 5493 (1959).

13) T. Masamune, A. Murai, O. Orito, H. Ono, S. Numata, and H. Suginome, *Tetrahedron*, **25**, 4853 (1969).

14) If epimerization occurred at C_9, the 19-methyl protons of **20** had to appear in much lower field than those of **18**. *Cf.*, D. M. Bailey, D. P. G. Hamon, and W. S. Johnson, *Tetrahedron Lett.*, **1963**, 555; J. P. Kutney, A. By, T. Inaba, S. Y. Leong, *ibid.*, **1965**, 2911.

15) H. Suginome, N. Sato, and T. Masamune, *Tetrahedron Lett.*, **1969**, 2671.

16) W. F. Johns and I. Laos, *J. Org. Chem.*, **30**, 123 (1965).