The Transformation of Jervine into 18-Functional *D*-Homo-*C*-norsteroids. IV.[1] The Transformation of Jervine into (20*R*)-18,20β-Epoxy-3β-hydroxy-17β-ethyletiojervan-18-one 3-Acetate *via* (20*R*)-18,20β-Epoxy-3β-hydroxy-12α,17β-ethyletiojervan-11-one 3-Acetate[2]

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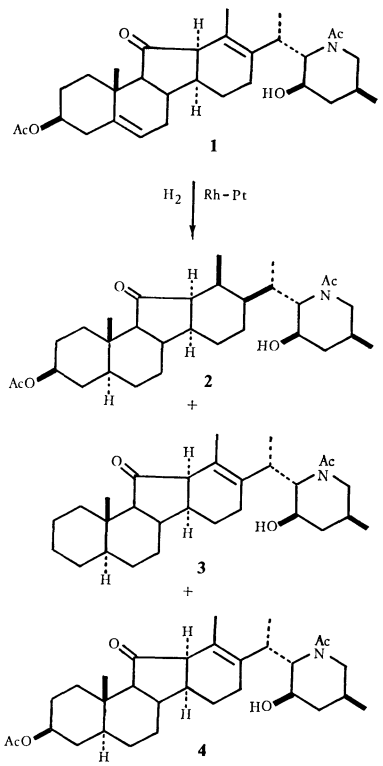
Catalytic hydrogenation of (22*S*,25*S*)-*N*-acetyl-3β,23β-dihydroxyveratra-5,13(17)-dien-11-one 3-acetate over rhodium-platinum catalyst in acetic acid gave (22*S*,25*S*)-N-acetyl-3β,23β-dihydroxyveratranin-11-one 3-acetate (**2**) in *ca* 70% yield, together with two minor products. Irradiation of **2** in benzene containing mercury(II) oxide and iodine gave 20-formyl-3β-hydroxy-12α,17β-ethyletiojervan-11-one 3-acetate (**5**) in 43% yield, accompanied by the 17-epimer of (22*S*,23*R*,25*S*)-N-acetyl-3β-hydroxy-5α-jervanin-11-one 3-acetate (4%). Aldehyde **5** was transformed into 3β-hydroxy-12α,17β-ethyletiojervane-11,20-dione 3-acetate (**15**) (79% yield) by photo- or copper-catalysed oxygenation of the corresponding enamine. Reduction of **15** with sodium borohydride gave 3β,20β-dihydroxy-12α,17β-ethyletiojervan-11-one 3-acetate (**17**) as a major product (69%), together with the 20-epimer. The hypoiodite reaction of **17** gave 18,20β-epoxy-3β-hydroxy-17β-ethyl-12α-etiojervan-11-one 3-acetate (**19**) in 92% yield. Hydrolysis of **19** resulted in the isomerization of the C/D ring junction to give 18,20β-epoxy-3β-hydroxy-17β-ethyletiojervan-11-one (**20**), the first 18-functional C/D *trans* *D*-homo-*C*-norsteroid ever prepared. Wolff-Kishner reduction of **20** gave the corresponding 11-deoxo compound; its acetylation followed by oxidation yielded 18,20β-epoxy-3β-hydroxy-17β-ethyletiojervan-18-one 3-acetate. The 11-oxo function of **19** can be reduced quite easily with lithium aluminum hydride to give the corresponding 11β-ol.

Despite the extensive studies on the synthesis of 18-functional steroids, little has been done on the synthesis of 18-functional *D*-homo-*C*-norsteroids which may be useful for the synthesis of biologically active compounds. In the previous paper,[1] we reported the transformation of jervine into 18-functional C/D *cis* fused *D*-homo-*C*-norsteroids.

In this paper, the transformation of jervine into an 18-functional C/D *trans* fused *D*-homo-*C*-norsteroid, (20*R*)-18,20β-epoxy-3β-hydroxy-17β-ethyletiojervan-18-one 3-acetate,[3] *via* a C/D *cis* fused 11-oxo-*D*-homo-*C*-norsteroid, is reported. The method involved a series of photoinduced reactions reported in the previous paper.[1]

Results

Catalytic hydrogenation of (22*S*,25*S*)-*N*-acetyl-3β,23β-dihydroxyveratra-5,13(17)-dien-11-one 3-acetate (**1**), derived from jervine *via* two steps,[4] over rhodium-platinum catalyst in acetic acid[1,5] gave a mixture of products from which a perhydro derivative, (22*S*,25*S*)-*N*-acetyl-3β,23β-dihydroxyveratranin-11-one 3-acetate (**2**), was obtained by a single recrystallization in 62% yield (Scheme 1). Hydrogenation of the mixture recovered from the reaction gave a further amount (10%) of perhydro derivative **2**. The structure of **2** was confirmed by the IR, NMR, and mass spectra. The NMR spectrum (Table 1) showed the absence of an olefinic proton and showed three doublets arising from three secondary methyl groups (the 18-H, 21-H, and 26-H). The assigned stereochemistry at C-5, C-13, and C-17 centers is based on a *cis* addition analogous to the closely related substrate.[1,4] TLC of the crude product in this catalytic hydrogenation indicated the presence of two minor products **3** and **4**, which are more mobile than the perhydro derivative **2**. The structure of crystalline product **3**, mp 218.5—219.5 °C, was ascertained to be (22*S*,25*S*)-*N*-acetyl-23β-hydroxyveratr-13(17)-en-11-one by the mass, IR, and NMR spectra. Its mass spectrum showed a M^+ peak at *m/e* 455 and a fragment ion of low abundance at *m/e* 299 due to a species resulting from the removal of the heterocyclic ring from the molecular ion. Its IR spectrum showed bands due to the 23β-hydroxyl, 11-oxo- and *N*-acetyl groups. The NMR spectrum showed no 3β-acetoxyl



Scheme 1.

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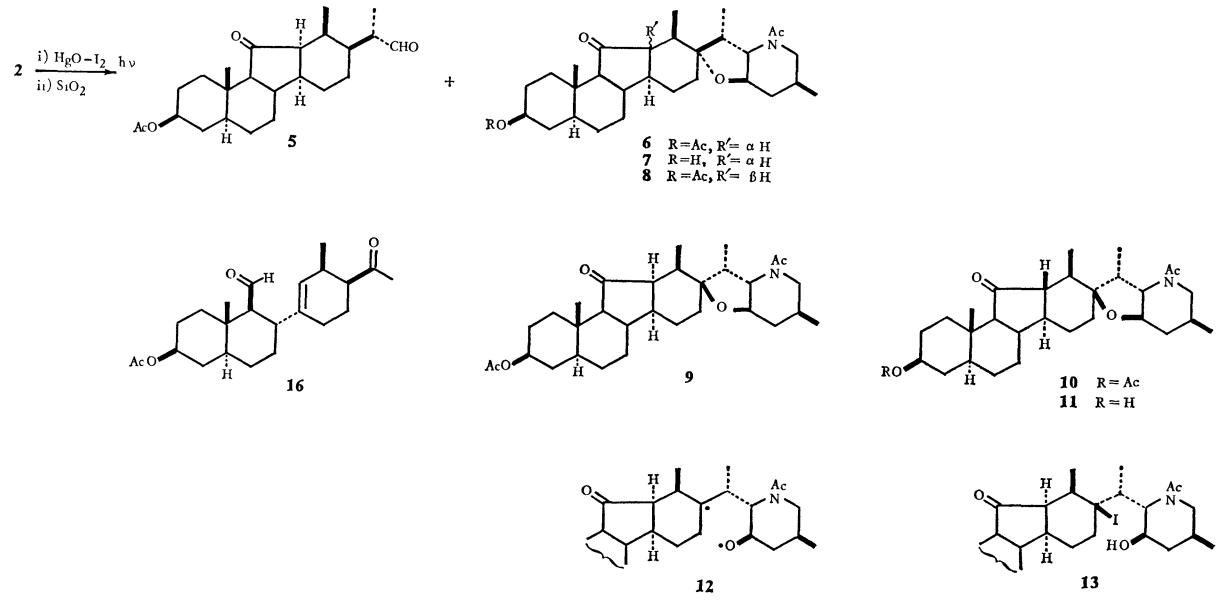
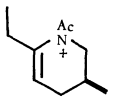


Scheme 2.

group and the presence of a 3H singlet at τ 8.14 due to the 18-H.

The structure of the amorphous product **4** was shown to be (22*S*,25*S*)-*N*-acetyl-3β,23β-dihydroxyveratr-13(17)-en-11-one 3-acetate by spectrometry. The mass spectrum showed a M^+ peak of *m/e* 513. The IR spectrum showed bands due to the 23β-hydroxyl, 11-oxo-, *N*-acetyl, and 3β-acetoxyl groups. The NMR spectrum showed a three-proton singlet at τ 8.14 due to the 13-methyl group and the absence of olefinic protons, proving the product to be the 5,6-dihydro derivative of the starting diene.

The transformation of the perhydro derivative **2** into a 12α-etiojervane **15** was accomplished by the series of photoinduced reactions described in the previous paper.[1,6] (Schemes 2 and 3) Irradiation of **2** in benzene containing three equivalents each of mercury(II) oxide and iodine with a 100-W high pressure mercury arc gave the expected crystalline aldehyde, 20-formyl-3β-hydroxy-12α,17β-ethyletiojervan-11-one 3-acetate (**5**), mp 144—146 °C, in 43% yield after column chromatography with silicic acid and recrystallization. The various spectra were in agreement with the structure assigned. The TLC of the crude photolysate showed the formation of a very minor product **6**, which was more mobile than aldehyde **2**. It was isolated by column chromatography in 4% yield and had mp 219—220 °C. Its mass spectrum (M^+ 513) and the elemental analysis were in agreement with the molecular formula $C_{31}H_{47}O_5N$, indicating it to be a product from an intramolecular hydrogen abstraction by a 23β-oxyl radical arising from the 23β-ol **2**. Hydrogens available for the intramolecular abstraction by the oxyl radical would be the 16α-H, the 17-H, and the 21-H and the abstraction reactions involving these hydrogens should take place *via* six or seven-membered cyclic transition state.[7] The ^{1}H NMR spectrum of **6** showed three three-proton doublets assigned to the 18-H, 21-H, and 26-H, excluding any structure arising from the abstraction of the 21-H. The ^{13}C NMR spectrum of **6**, aided with off-resonance spectrum, showed a signal at δ 86.64 ppm ascribed to a quarternary carbon carrying an oxygen.[8] This result proved that the 23β-oxyl radical abstracted the 17α-H, resulting in a N-acetyltetrahydrojervine O-acetate, the signal at 86.64 ppm thus arises from the C-17. A tetrahydro derivative of jervine, (22*S*, 23*R*, 25*S*)-*N*-acetyl-3β-hydroxy-5α-jervanin-11-one acetate, (**9**) and its 12β-isomer (**10**) (the C-17 signal at δ 86.52 ppm) have already been prepared by catalytic hydrogenation of jervine in acetic acid followed by acetylation.[9,10] The direct comparison showed that **6** is not identical with *N*-acetyltetrahydrojervine **9**.[9] Therefore, the structure of **6** should be the 17-epimer of (22*S*,23*R*,25*S*)-*N*-acetyl-3β-hydroxy-5α-jervanin-11-one 3-acetate. The mass spectra of **6** and **10** showed their base peaks at *m/e* 167 could be assigned to a fragment of structure (A)[11]



(A)

in accordance with the assigned structure. Hydrolysis of **6** with aqueous methanolic potassium hydroxide under reflux gave the corresponding 3β-ol (**7**). The C/D ring junction of **7** was proved to be *cis*, since **7** reverted back to **6** on acetylation. It is noteworthy that, while treatment of (22*S*,23*R*,25*S*)-*N*-acetyl-3β-hydroxy-5α-jervanin-11-one 3-acetate (**9**) with base readily causes an epimerization at the C-12 and gives the 12β-epimer (**11**), no isomerization of the C-12 hydrogen takes place in the basic hydrolysis of **6**. Inspection of Dreiding models of **6** and its 12β-epimer **8** showed that the most stable conformation of the ring D of **6** would be a *quasi* chair conformation with the 13-axial substituent, but that of the 12β-epimer **8** would be a *quasi* chair conformation with the 13-equatorial substituent. It also showed that the 13β-

Table 1. NMR parameters for
[chemical shifts (τ) and

Compound	3α-H	6-H	11α-H (11-H)	12α-H	18-H	19-H
1	5.44, br	4.62, bs	—	7.18, d (7.5)	8.15, s	9.02, s
2	5.36, br	*	—	*	9.29, d (6.0)	9.13, s
3	*	*	—	7.24, d (9.0)	8.14, s	9.23, s
4	5.39, br	*	—	7.23, d (9.0)	8.14, s	9.21, s
5	5.35, br	*	—	*	9.26, d (6.0)	9.10, s
6	5.34, br	*	—	*	9.21, d (6.0)	9.12, s
14	5.35, br	*	—	*	9.35, d (7.2)	9.10, s
15	5.45, br	*	—	*	9.34, d (7.5)	9.15, s
16	5.30, br	*	0.55, d (5.4)	4.52, d (3.0)	9.23, d (7.5)	8.93, s
17	5.33, br	*	—	*	8.80, d (6.0)	9.11, s
18	5.35, br	*	—	*	8.83, d (6.0)	9.11, s
19	5.36, br	*	—	*	18β-H, 6.84, dd, (10.5, 7.5) 18α-H, 6.12, t, (7.5)	9.17, s
20	6.43, br	*	—	*	18β-H, 5.64, d, (8.6) 18α-H, 6.17, dd, (8.6, 4.9)	9.18, s
21	—	*	—	*	18β-H, 5.75, d, (8.7) 18α-H, 6.15, dd, (8.7, 4.8)	8.99, s
22	a)	*	*	*	18β-H, 6.38, d, (8.4) 18α-H, 6.19, dd, (8.4, 4.8)	9.29, s
23	5.28, br	*	*	*	18β-H, 6.37, d, (8.4) 18α-H, 6.16, dd, (8.4, 4.8)	9.25, s
24	5.37, br	*	*	*	—	9.33, s
25	6.38, br	*	*	*	—	9.30, s
26	6.41, br	*	5.68, t (6.0)	*	18α- and β-H 6.07, s ($W1/2=5$)	8.99, s
27	5.33, br	*	5.70, t (6.0)	*	18α- and β-H 6.09, s ($W1/2=5$)	8.98, s
28	—	*	5.64, t (6.3)	*	18α- and β-H 6.09, s ($W1/2=5$)	8.80, s

a) Superimposed on 18-H. b) Superimposed on 18α-H. c) *d*, (9.0) after irradiation at τ 8.80. d) *d*, (9.3)

methyl and the 20α-methyl of **8** are nearly in a 1,3-diaxial relationship and therefore the 12β-epimer **8** (C/D *trans* isomer) appears to be less stable than the 12α-epimer **6**, in which the C(13)–C(18) and C(20)–C(21) bonds are in nearly orthogonal positions. On the other hand, there are no non-bonded interactions between the 13β-methyl and the 20α-methyl of **9** and its 12β-epimer **10**. Thus, the situation differs sharply from that of the pair of 17-epimers **6** and **8**.

The jervanine **6** may be formed *via* an intramolecular radical combination of a biradical intermediate **12**. In this step, the attack of the 23β-oxyl radical to the C-17 radical center from the β-face should be hindered by the presence of the 13β-methyl group and therefore the observed product **6** will result. The formation of **6** through an iodohydrin intermediate (**13**) is unlikely, since the combination of an iodine atom with the C-17 radical from the β-face would be severely hindered by the 13β-methyl group.

The aldehyde **5** was transformed into a crystalline enamine **14** with morpholine and *p*-toluenesulfonic acid in toluene under reflux in an almost quantitative yield. The enamine **14** was then subjected to a copper-catalysed oxygenation[12] or an oxidative cleavage with

ETIOJERVANE DERIVATIVES IN $CDCl_3$
splittings (Hz; in parentheses)]

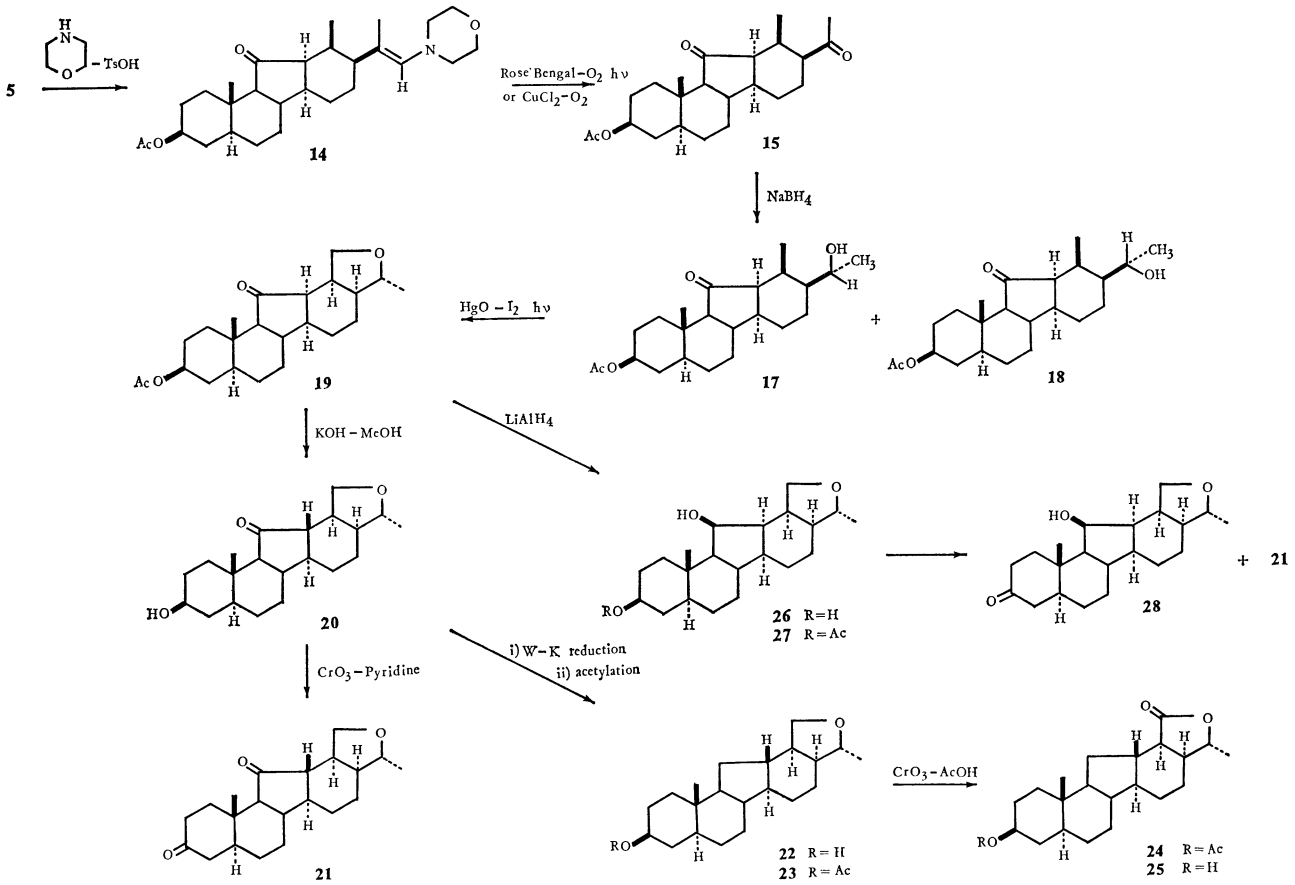
20-H	21-H	22α-H (22-H)	23α-H	26-H	27-H	NAc, OAc
6.97, dq (6, 11)	8.83, d (6.3)	5.33, bd (10.5)	5.92, bs ($W1/2=7.5$)	9.02, d (6.5)	6.80, bs ($W1/2=6.6$)	8.00, s, and 8.03 s,
*	9.13, d (5.4)	6.72, bs	6.05, bs ($W1/2=18$)	8.95, d (6.0)	*	7.90, s, and 8.01, s
7.00, dq (6, 11)	8.85, d (6.3)	5.38, bd (11.3)	5.95, bs ($W1/2=7.5$)	8.98, d (6.6)	6.80, bs	7.98, s
7.00, dq (7, 12)	8.85, d (6.3)	5.39, d (10.5)	5.95, bs ($W1/2=7.5$)	8.99, d (6.6)	6.80, bs	8.00, s
*	8.98, d (7.2)	0.45, d	—	—	—	7.98, s
*	9.08, d (6.0)	*	*	9.01, d (6.6)	*	7.92, s, and 7.98, s
—	8.35, s	4.78, s	—	—	—	8.01, s
—	7.94, s	—	—	—	—	8.04, s
—	7.89, s	—	—	—	—	7.98, s
6.43, dq	9.20, d (6.6)	—	—	—	—	8.00, s
6.45, m	9.27, d (6.6)	—	—	—	—	8.00, s
6.32, dq	8.82, d (6.3)	—	—	—	—	8.00, s
ca. 6.2 b)	8.82, d (6.0)	—	—	—	—	—
6.18, dq c)	8.80, d (6.0)	—	—	—	—	—
a)	8.83, d (6.0)	—	—	—	—	—
a)	8.82, d (6.0)	—	—	—	—	8.01
5.65, dq d)	8.71, d (6.0)	—	—	—	—	8.07
5.60, dq (9.8, 6.0) e)	8.65, d (6.0)	—	—	—	—	—
6.12, dq (2.3, 6.0)	8.85, d (6.0)	—	—	—	—	—
6.12, dq	8.84, d (6.0)	—	—	—	—	7.99, s
6.13, dq (4.5, 6.0)	8.83, d (6.0)	—	—	—	—	—

after irradiation at τ 8.71. e) (9.8) after irradiation at τ 8.65.

dye-sensitized singlet oxygen[13] (Scheme 3).

In the copper-catalyzed oxygenation, oxygen was bubbled through a chloroform solution of the enamine **14** containing copper(I) chloride for 24 h under cooling. The expected product, 3β-hydroxy-12α,17β-ethyletiojervane-11,20-dione 3-acetate (**15**), mp 134—135 °C, was obtained in 91% yield after recrystallization from diethyl ether.

In the dye-sensitized oxidative cleavage, the enamine **14** in dry benzene containing Rose Bengal was irradiated with a 90-W high pressure mercury arc under an atmosphere of oxygen for 48 h. Column chromatography of the product gave dione **15**, which is identical with the dione obtained by the copper-catalyzed oxygenation, in 79% yield. Although this photochemical procedure was successful in most of the experiments with 90-W Hg arc, the irradiation was found in some experiments to lead to the exclusive formation of an aldehyde **16** resulting from α-fission of an excited 11-oxo group; in these experiments a lamp of a wattage slightly above 100-W was used. The structure of the aldehyde **16** was confirmed to be 3β-hydroxy-11,12-seco-17β-ethyletiojervane-11,20-dione 3-acetate by spectrometry. The high



Scheme 3.

resolution mass spectrum of **16** indicated that it had the molecular formula $C_{23}H_{34}O_4$. The IR spectrum of **16** showed three bands arising from the acetoxyl, the formyl, and the acetyl groups. The NMR spectrum showed two one-proton doublets at τ 0.55 (J= 5.4 Hz) and at τ 4.52 (J=3.0 Hz) assignable to the C-11 hydrogen and the olefinic C-12 hydrogen, and other signals consistent with the assigned structure. The use of the high pressure Hg arc lamps of wattage as intense as 100 watts for the oxygenation seems to be just on a critical line for the cleavage and may be inappropriate, even though the excited 11-oxo group is being quenched by oxygen during oxygenation, which is a faster process than the α-fission.

The 20-oxo group of the 11,20-dione **15** was selectively reduced with sodium borohydride in ethanol containing ethyl acetate to give a mixture of 3β,20β-dihydroxy-17β-ethyletiojervan-11-one 3-acetate (**17**) and its 20α-epimer (**18**). Recrystallization and preparative TLC of the mixture gave 20β-ol **17**, mp 169—171 °C, and 20α-ol **18**, mp 175—176 °C, in 69 and 11% yields respectively. It was not possible to deduce the configurations at the C-20 centers of these compounds by NMR spectroscopy, since the differences in the splitting and the chemical shifts of their 20-H signals and the differences in the chemical shifts of their 18-H were too small to distinguish the configurations of their C-20 centers. However, consideration of the steric course of the reduction with complex metal hydrides, in a manner analogous to the case of the reduction of the 11-deoxo analogue[5] of dione **15**, allowed us to assign a 20β-configuration for the major product and a 20α- for the minor one. These assignments were further supported by an analysis of the NMR spectrum of 18,20β-epoxy-3β-hydroxy-17β-ethyletiojervan-11-one 3-acetate (**19**) obtained by the hypoiodite reaction of the alcohol **17** (*vide infra*). Interestingly, the 11-oxo group of **15** exerts an influence on the steric course of the reduction, as shown by the formation of an appreciable amount of 20α-isomer **18** from **15** and the exclusive formation of 20β-isomer from a 11-deoxo analogue of **15**.[5]

The 20β-ol **17** in benzene containing mercury(II) oxide and iodine was then irradiated for 2.5 h under an argon atmosphere.[1,7b] Column chromatography of the product gave **19** in 81% yield together with the recovered material (7%). Various spectra of the product was in agreement with (20*R*)-18,20β-epoxy-3β-hydroxy-17β-ethyl-12α-etiojervan-11-one 3-acetate (**19**). Thus, high resolution mass spectrometry confirmed the molecular formula $C_{23}H_{34}O_4$. IR spectrum showed the absence of any hydroxyl group and the presence of a superimposed band at 1732 cm^{-1} arising from the 3β-acetoxyl and the 11-oxo groups. The very intense molecular ion peak (67.8%) in the mass spectrum of **19** contrasts to that of the 11-deoxo analogue,[5] in which the intensity of the molecular ion is only 2% and M^+-CH_3 ion peak is intense. The NMR spectrum showed a three-proton doublet at τ 8.82 with J=6.3 Hz assigned to the 21-H. It also

showed a one-proton double quartet at τ 6.32. Irradiation at τ 8.82 caused a collapse of the double quartet at τ 6.32 to a doublet with J=4.2 Hz. On this basis, the signal at τ 6.32 is asigned to the 20-H. The NMR spectrum showed another double doublet at τ 6.84 with J=10.5 Hz and 7.5 Hz and a triplet at τ 6.12 with J=7.5 Hz; these are assigned to the 18β-H and the 18α-H respectively. Model inspection indicates that the dihedral angles between the 18α-H and the 13α-H, and the 18β-H and the 13α-H in a twisted boat conformation of the ring D are about 20° and 140° respectively, in accord with the observed magnitudes of the couplings. The relevant coupling constants are $J_{18\alpha,18\beta}$=7.5 Hz, $J_{18\beta,13\alpha}$=7.5 Hz, and $J_{18\beta,13\alpha}$=10.5 Hz. The Dreiding molecular model also shows that the dihedral angle between the 17α-H and the 20β-H is about 120° in the above conformation. The observed coupling constant 4.2 Hz allows us to assign the configuration of the methyl group at the C-20 to be α. Therefore, **17** should be the 20β-ol.

Hydrolysis of **19** with methanolic potassium hydroxide gave a crystalline alcohol **20**, mp 229—229.5 °C, the first 18-functional C/D *trans* *D*-homo-*C*-norsteroid ever prepared. The epimerization of the C-12 center of **19** was proved by the ^{1}H NMR spectrum of **20**. The ^{1}H NMR spectra of **20** and 3-oxo compound **21** showed an appreciable change of the splitting of the signals arising from their 18-methylene protons, in comparison with the correponding ones of C/D *cis* compound **19**. The spectrum of **20** showed a broad doublet at τ 5.64 with J=8.6 Hz and a double doublet at τ 6.17 with J=8.6 Hz and 4.9 Hz. The inspection of the model of C/D *trans* ketone **20** having the ring D in a *quasi* chair conformation indicated that the dihedral angle between the 18β-H and the 13α-H is about 90° and that between the 18α-H and the 13α-H is about 30°. On the other hand, the two corresponding dihedral angles in the model of C/D *trans* ketone having the ring D in a boat conformation were about 130° and 30°. The observed coupling constants are thus in agreement with the predicted ones for the hydroxy ketone having the ring D in a chair; the doublet at τ 5.64 and the double doublet at τ 6.17 are ascribed to the 18β-H and the 18α-H. A signal due to the 20β-H was superimposed on the signal arising from the 18α-H; the superimposed signal shape changed when a three-proton doublet at τ 8.82 (the 21-H) was irradiated. The isomerization of the C/D junction of **19** in the hydrolysis was finally confirmed by a comparison of its 11-deoxo compound (**23**) with (20*R*)-18,20β-epoxy-17β-ethyl-12α-etiojervan-3β-ol 3-acetate[1,5] previously prepared. This showed that the two compounds are not identical (*vide infra*).[1,5]

The ketone **20** was then oxidized to 18,20-epoxy-17β-ethyletiojervane-3,11-dione (**21**) with chromium trioxide-pyridine. Oxidation of **21** with chromium trioxide-acetic acid failed to give the lactone. It is almost certain that the 11-oxo group hinders the oxidation of the 18-methylene to a 18-oxo group, since the 18-methylene group of the corresponding 11-deoxo compound (**23**) can readily be oxidized to 18-oxo group (*vide infra*).

The 11-oxo group of **20** was removed by a modified procedure[14] of the Wolff-Kishner reduction. The reduction by this procedure gave 11-deoxo alcohol (**22**), mp 171—174 °C, as a single product. It gave an O-acetyl derivative (**23**), which was proved to be not identical with 18,20β-epoxy-17β-ethyl-12α-etiojervan-3β-ol 3-acetate reported previously.[1,5] The NMR spectra of **22** and **23** showed that the splittings of the signals arising from their 18-methylene protons were similar to those of their 11-oxo analogue **20**, with the exception that the doublet arising from the 18β-H shifted significantly to a higher field (Δ 0.74 ppm for **22**). Oxidation of **23** with chromium trioxide in acetic acid gave an amorphous γ-lactone (**24**) in 39% yield. The IR spectrum showed two bands due to an acetoxyl and a γ-lactone groups. Its NMR spectrum exhibited a double quartet at τ 5.65 due to the 20β-H and a doublet at τ 8.71 due to the 21-H. Irradiation at τ 8.71 caused a collapse of the former to a doublet with J=9.3 Hz. The mass spectrum showed only a weak molecular ion peak at *m/e* 374 (0.3%), a base peak at *m/e* 314, and a prominent peak at *m/e* 299 (35.7%). The last two fragments are attributable to $M^+-CH_3CO_2H$ and $M^+-CH_3CO_2H-CH_3$.

Hydrolysis of the lactone **24** in a mixture of chloroform and methanol with dilute hydrochloric acid at room temperature gave the corresponding 3β-ol **25**, mp 202—205 °C.

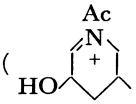
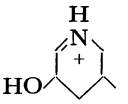
The aforementioned experiments indicated that the cyclic ether **19** with the C/D *cis* junction is a less stable isomer and readily isomerizes with a base to the more stable cyclic ether **20** with C/D *trans* junction. Attempts have been made to modify the 11-oxo function of **19** without affecting the stereochemistry of the C/D *cis* ring junction. Reduction of the 11-oxo function of **19** with lithium aluminum hydride for 1.5 h at room temperature gave 3β,11β-diol (**26**), mp 211—214 °C, as a single product. This remarkably facile reduction of the 11-oxo group is surprising. The conformation of the molecule **19** should be one in which the degree of steric hindrance around the 11-oxo group for the attack of hydride ion is appreciably reduced. The *cis* stereochemistry of the C,D-ring junction was supported by NMR spectroscopy. The NMR spectrum showed a one-proton triplet at τ 5.68 (J=6.0 Hz) assigned to the 11α-H, a two-proton singlet ($W_{1/2}$= 5 Hz) at τ 6.07 assigned to the 18-methylene protons, and a one-proton double quartet centered at τ 6.12 with J=2.3 and 6.0 Hz ascribed to the 20β-H. Apart from these signals it showed a one proton multiplet centered at τ 7.49 and a three-proton doublet at τ 8.85 (J=6.0 Hz) ascribed to the 17α-H and the 21-H. These assignments were supported by the following spin decoupling studies. Irradiation at τ 8.85 resulted in a collapse of the double quartet at τ 6.12 into a doublet with J=2.3 Hz. Irradiation at τ 7.49 decoupled the double quartet at τ 6.12 into a quartet with J=6.0 Hz. Finally, irradiation at τ 6.12 resulted in collapses of the doublet at τ 8.85 to a singlet and of the multiplet at τ 7.49 into a diffused triplet. On the basis of these results, the relevant coupling constants are $J_{21\text{-H},\ 20\beta\text{-H}}$=6.0 Hz, $J_{20\beta\text{-H},\ 17\alpha\text{-H}}$=2.3

Hz, $J_{18\alpha\text{-H},\,18\beta\text{-H}} \simeq J_{18\alpha\text{-H},\,13\alpha\text{-H}} \simeq J_{18\beta\text{-H},\,13\alpha\text{-H}} < 5$ Hz. The unusually small gem-coupling of the 18-methylene protons should be noted.

Acetylation of **26** by the standard procedure gave a 3-acetate **27**. To transform 3β-hydroxyl group into a 3-oxo group, diol **26** was subjected to the Oppenauer oxidation. However only a low yield of 3-oxo compound **28** was obtained, together with 3,11-dione **21**. An analysis of the signals arising from the 18-methylene protons and the 20β-proton of **28** is given in the Table.

Experimental

For instruments used and general procedures see Ref. 1. Low resolution mass spectra of compounds **2,4—7**, **14**, **15**, **17**, **18**, **20—26**, and all the high resolution mass spectra were recorded at the Faculty of Agriculture of this University with a Hitachi JMS-D 300 spectrometer. Low resolution mass spectra of compounds **3**, **18**, and **28** were recorded at the Faculty of Pharmaceutical Sciences with a Hitachi RMU-6E spectrometer.

*Catalytic Hydrogenation of (22S,25S)-N-Acetyl-3β,23β-dihydroxyveratr-5,13(17)-dien-11-one 3-Acetate (**1**).* (*a*): Rhodium–platinum catalyst (38.65 g) in glacial acetic acid (350 ml) was shaken under an atmosphere of hydrogen for *ca.* 11.5 h. To this solution was added the diene **1** (25.0 g) dissolved in glacial acetic acid (250 ml). The resulting solution was shaken under an atmosphere of hydrogen for 43.5 h and then a further amount of freshly prepared catalyst (4 g) in glacial acetic acid (150 ml) was added. The solution was again shaken under an atmosphere of hydrogen for 18.5 h. During this period, 3.25 l of hydrogen were absorbed. After the removal of the catalyst and the solvent, water (300 ml) was added to the residue and the solution was neutralized with aq 10% sodium carbonate solution. The solution was then extracted with chloroform (500 ml × 3). The chloroform solution was washed with water and dried. After the usual work-up, the residue was recrystallized from acetone–diethyl ether to yield perhydro derivative **2**, mp 204—206 °C. (15.60 g) in colorless crystals in two crops. (Found: C, 72.24; H, 9.75; N, 2.67%. Calcd for $C_{31}H_{49}NO_5$: C, 72.19; H, 9.58; N, 2.72%); $[\alpha]_D^{25}$ −1.5° (*c* 1.5, $CHCl_3$); IR, 3319 (OH), 1734 and 1722 (5-membered ring ketone and OAc), 1606 (NAc), 1236 and 1015 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*), 515 (M^+, 0.4), 500 (M^+-CH_3, 0.3) 472 (0.3), 198 (0.3), 185 (0.7), 156 ( , 100), and 114 ( , 17.3); for NMR see Table 1.

Examination of the residue (9.4 g) from the filtrate by TLC indicated that it was a mixture of the starting material, which was the major component, and two other minor products. This residue in glacial acetic acid (200 ml) was again hydrogenated in the presence of rhodium–platinum catalyst (14.4 g). About 0.74 l of hydrogen were absorbed during 50 h. The product was recrystallized from diethyl ether to yield perhydro derivative **2** (0.794 g). The residue from the filtrate was subjected to column chromatography (Mallinckrodt silicic acid, 100 mesh, 100 g). Elutions with hexane, benzene, and a 1:1 mixture of chloroform and benzene gave a mixture (6.85 g). An analysis of a part of the mixture by preparative TLC (a 5:3 mixture of diethyl ether–chloroform as the solvent) indicated that it contained 1.01 g of perhydro derivative **2**. Further elutions with diethyl ether gave a fraction which gave the perhydro derivative **2** (0.505 g) after recrystallization from diethyl ether. The total yield of perhydro derivative **2** was thus 71.6%. Isolations of the minor products **3** and **4** are described in the following procedure (b).

(*b*): Rhodium–platinum catalyst (2.0 g) in glacial acetic acid (30 ml) was shaken under an atmosphere of hydrogen for 4 h. During this period, 578 ml of hydrogen were absorbed. To this solution was added diene **1** (2 g) in glacial acetic acid (30 ml) and the solution was shaken under an atmosphere of hydrogen for 46 h, 180 ml of hydrogen being absorbed. After removal of the catalyst and the solvent, the product was dissolved in chloroform and the solution was washed with water, then dried over anhydrous sodium sulfate. The residue (2.472 g) showed four spots on TLC (a 5:3 mixture of diethyl ether–chloroform). A part of the product (750 mg) was subjected to preparative TLC with a 5:3 mixture of diethyl ether and chloroform to give four fractions: A (69 mg), B (337 mg), C (62 mg), and D (388 mg) in the order of decreasing mobility. Fraction A was recrystallized from acetone–diethyl ether to yield product **3**, mp 218.5—219.5 °C (15 mg). (Found: C, 76.54; H, 9.94; N, 3.14%. Calcd for $C_{29}H_{45}O_3N$: C, 76.44; H, 9.95; N, 3.07%); IR 3314 (OH), 1725 (5-membered ring ketone), 1608 (NAc), 1254, and 1017 cm^{-1}; MS (80 eV), *m/e* (*rel intensity*), 455 (M^+, 0.3), 299 (1), 298 (0.9), 156 (100), 114 (45), 55 (9), and 43 (9); for NMR see Table 1.

Fraction B was identified as an olefin **4** but could not be induced to crystallize. (Found: *m/e* 513.3453. $C_{31}H_{47}NO_5$ requires M^+ 513.3453); $[\alpha]_D$ +1.64° (*c*, $CHCl_3$); IR, 3320 (OH), 1727 (OAc and 5-membered ring ketone), 1604 (NAc), 1240, and 1028 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*), 513 (M^+, 0.2), 357 (M^+—C—20 substituent, 0.5), 156 (100), and 114 (20.6); for NMR see Table 1.

Fraction C was a mixture; fraction D was recrystallized from acetone–diethyl ether to yield perhydro derivative **2**, (238 mg).

*The Removal of Heterocyclic Moiety of (22S,25S)-N-Acetyl-3β,23β-dihydroxyveratranin-11-one 3-Acetate **2** by Irradiation in the Presence of Mercury(II) Oxide and Iodine.* The perhydro compound **2** (13.5 g) in dry benzene (700 ml) in the presence of mercury(II) oxide (27.0 g) and iodine (33.8 g) was irradiated with a 100-W high pressure mercury arc while being stirred. After a period of 24 h, more iodine (3 g) and mercury(II) oxide (3 g) were added and the irradiation was continued for another 24 h. Precipitates were removed by filtration and washed with hot benzene. The solution and the washing were combined, washed with saturated aq sodium hydrogensulfite solution (300 ml) and water (500 ml × 2), and dried over anhydrous sodium sulfate. Removal of the solvent at below 40 °C gave a brown residue. TLC indicated that this was largely aldehyde **5**, together with a small amount of a less mobile compound **6**. The residue was subjected to column chromatography with Mallincrodt silicic acid (35 g). Elutions with a 1:1 mixture of benzene and hexane and then benzene only gave three fractions. The first fraction gave crystalline aldehyde **5**. Recrystallization from diethyl ether gave pure aldehyde **5** (4.0 g), mp 144—146 °C (Found: *m/e* 388.2608. Calcd for $C_{24}H_{36}O_4$: M^+ 388.2613); $[\alpha]_D^{25}$ −3.3° (*c* 0.4, $CHCl_3$); IR, 1731, (broad, CHO, OAc and 5-membered ring ketone), 1234, and 1020 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*) 388 (M^+, 34.1), 360 (M^+—CO, 52.7), 345 (9.3), 330 (M^+—C—17 substituent-H, 17.7), 328 ($M^+-CH_3CO_2H$, 39.5), 300 ($M^+-CO-CH_3CO_2H$, 77.4), 147 (89.0), 123 (70.3), 95 (73.2), 93 (87.8), 81 (75.8), 67 (61.8), 55 (70.4), and 43 (100); for NMR see Table 1.

The second fraction gave an amorphous mixture (800 mg), which was subjected to preparative TLC with a 20:1 mixture of chloroform and diethyl ether to give aldehyde **5** (300 mg) and a new compound **6** (479 mg). The aldehyde **5** was recrystallized from diethyl ether to give a pure specimen (259 mg). The new compound **6** was recrystallized from diethyl ether to give a pure specimen, mp 221—222 °C. (Found: C, 72.25; H, 9.18; N, 2.58%. Calcd for $C_{31}H_{47}NO_5$; C, 72.48; H, 9.22; N, 2.73%); $[\alpha]_D^{25}$ −2.7 (*c* 1.1, $CHCl_3$); IR, 1733 (OAc and 5-membered ring ketone) and 1671 cm^{-1} (NAc); MS, (70 eV) *m/e* (*rel intensity*), 513 (M^+, 11.9), 277 (5.2), 222 (20.3), 211 (31.5), 167 (100), 156 (24.5), 114 (9.8), and 43 (17.3); for NMR see Table 1.

Hydrolysis of Compound ***6***. Product **6** in methanol (5 ml) containing potassium hydroxide (250 mg) was heated under reflux and an atmosphere of nitrogen for 40 min. After the removal of methanol, water (20 ml) and 2 mol dm^{-3} hydrochloric acid (5 ml) were added to the residue. The solution was extracted with chloroform. The organic layer was worked up as usual. The amorphous residue (41 mg) was recrystallized from acetone–diethyl ether to give 3β-ol **7**, mp 242—244°. (Found: *m/e* 471.3334. Calcd for $C_{29}H_{45}NO_4$: M^+ 471.3346); MS ,(70 eV) *m/e* (*rel. intensity*), 471 (M^+, 19.7), 222 (18.5), 211 (31.2), 167 (100), and 156 (19.1).

Preparation of Enamine ***14*** *from 20-Formyl-3β-hydroxy-12α-17β-ethyletiojervan-11-one 3-Acetate.* Aldehyde **5** (4 g), morpholine (10 ml), and p-toluenesulfonic acid (200 mg) in dry toluene (150 ml) were heated under reflux in a flask fitted with a Dean Stark trap for 5.5 h. After the removal of the solvent, an oily residue was extracted with chloroform (200 ml×2). The solution was washed with an aq 5% sodium carbonate solution (100 ml) and water (100 ml×2) and dried over anhydrous sodium sulfate. Removal of the solvent left crystals of enamine **14** (4.45 g), mp 106—108 °C. This enamine **14** was used immediately for the next step without further purification. (Found: *m/e* 457.3203. Calcd for $C_{28}H_{43}NO_4$: M^+ 457.3192); $[\alpha]_D^{25}$ −4.4 (*c* 1.1, $CHCl_3$); IR, 1732 (OAc and 5-membered ring ketone), 1260, 1123, 1031, 874, and 735 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*) 457 (M^+, 72.0), 388 (11.2), 360 (18.9), 328 (18.5), 300 (31.3), 166 (100), 147 (38.9), 123 (34.3), 100 (43.9), 95 (44.3), 93 (42.8), 81 (39.4), 67 (31.2), 55 (36.6), and 43 (70.0); for NMR see Table 1.

*Preparation of 3β-Hydroxy-12α,17β-ethyletiojervane-11,20-dione 3-Acetate (****15****) from Enamine* ***14***. (*a*): Enamine **14** (500 mg) and copper(I) chloride (300 mg) in chloroform (100 ml) were cooled with ice–water and oxygen was bubbled through the solution for 9.5 h. After about 3 h, precipitates appeared in the yellow-green solution. At this point 10 ml of chloroform were added and the solution was allowed to stand under an atmosphere of oxygen for an additional 14.5 h. The precipitates were removed by filtration and washed with chloroform (100 ml). The filtrate and the washings were combined and worked up in the usual way. The crystalline residue was recrystallized from diethyl ether to yield dione **15** (343 mg), mp 134—135 °C. (Found: C, 73.99: H, 9.42%. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15%); $[\alpha]_D^{25}$ −1.4 (*c* 1.0, $CHCl_3$); IR, 1732 (OAc and 5-membered ring ketone), 1704 (Ac), 1242, 1024, 992, and 896 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*) 374 (M^+, 77.7), 359 (M^+-CH_3, 4.8), 314 ($M^+-CH_3CO_2H$, 19.5), 299 ($M^+-CH_3CO_2H-CH_3$, 25.2), 219 (9.8), 205 (10.3), 147 (18.3), 107 (14.7), 105 (16.6), 95 (57.3), 93 (20.3), 91 (15.8), 81 (15.5), 79 (16.4), 67 (17.7), 55 (17.4), and 43 (100); for NMR see Table 1.

(*b*): Enamine **14** (4.276 g) and Rose Bengal (100 mg) in dry benzene (600 ml) were irradiated with a 90-W high pressure mercury arc under an atmosphere of oxygen for 48 h. Oxygen was occasionally bubbled into the stirred solution. The solution was washed with water (300 ml×3) and dried over anhydrous sodium sulfate. After removal of the solvent, the crystalline residue (4.744 g), which was almost a single product, was subjected to column chromatography (Mallincrodt SiO_2, 7 g) to remove some polar substances. Elutions with benzene containing an increasing amount of chloroform gave dione **15**. It was recrystallized from diethyl ether to give 2.79 g in two crops.

(*c*): Enamine **14** (8.95 g) and Rose Bengal (250 mg) in dry benzene (1.3 l) were irradiated with a 103-W high pressure mercury arc for 48 h while oxygen was bubbled through slowly. After work-up as in procedure (b), the product (6.35 g) was subjected to column chromatography (Mallincrodt SiO_2, 15 g). Elutions with benzene gave a fraction which was recrystallized from diethyl ether–hexane to yield aldehyde (**16**) (3.4 g). The residue from the filtrate was subjected to preparative TLC with 50:1 chloroform–diethyl ether to yield a further amount of aldehyde (16) (0.31 g), mp 132—134 °C. (Found: *m/e* 374.2447. Calcd for $C_{23}H_{34}O_4$. M^+ 374.2455). IR, 1738 (OAc), 1726 (CHO), 1717 ($COCH_3$), and 1248 cm^{-1}. MS, *m/e* (*rel intensity*), 374 (M^+, 3.2), 346 (3.0), 286 (2.8), 271 (3.6), 253 (3.8), 107 (22.0), 105 (14.5), 95 (14.9), 93 (16.3), and 43 (100).

Reduction of Dione **15** *with Sodium Borohydride.* Dione **15** (600 mg) in absolute ethanol (60 ml) containing sodium borohydride (260 mg) and ethyl acetate (2 ml) was stirred for 2.5 h at room temperature. The reaction mixture was worked up as usual to give a residue (713 mg). Examination of the product by TLC with a 1:20 mixture of diethyl ether–chloroform showed it to be a mixture of a major product (R_f 4.4) and a minor product (R_f 5.5). Recrystallization from diethyl ether gave 3β,20β-dihydroxy-12α,17β-ethyletiojervan-11-one 3-acetate **17**, mp 169—171 °C, (349 mg). (Found: C, 73.22; H, 9.59%. Calcd for $C_{23}H_{36}O_4$. C, 73.36; H, 9.64%); $[\alpha]_D^{25}$ −0.62 (*c* 1.7, $CHCl_3$); IR, 3544 (OH), 1724 (OAc and 5-membered ring ketone), 1235, 1121, 1031, and 899 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*), 376 (M^+, 2.4), 358 (M^+-H_2O), 332 (45), 272 (100), 235 (27.4), 218 (31.8), 147 (43.9), 123 (32.4), 107 (36.1), 105 (32.6), 95 (92.2), 93 (58.5), 91 (31.9), 81 (41.6), 79 (36.2), 67 (40.6), 55 (38.4), and 43 (73.9); for NMR see Table 1.

Removal of the solvent from the filtrate gave a mixture of 20α- and 20β-ols (283 mg). The mixture was subjected to preparative TLC with a 1:20 mixture of diethyl ether–chloroform to give two fractions. The less mobile fraction (124 mg) was 20β-ol; this was recrystallized from diethyl ether to give pure 20β-ol **13** (64 mg). The more mobile fraction (68 mg) was recrystallized from diethyl ether to give 20α-ol **18**, mp 175—176 °C. (Found: C, 73.13; H, 9.54%. Calcd for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64%); $[\alpha]_D^{25}$ −1.1 (*c* 1.2, $CHCl_3$); IR 3564 (OH), 1726 (OAc and 5-membered ring ketone), 1232, 1106, 1019, and 895 cm^{-1}; MS, (80 eV) *m/e* (*rel intensity*) 376 (M^+, 4), 358 (M^+-H_2O, 8), 332 (29), 272 (78), 218 (57), 177 (30), 147 (54), 123 (43), 107 (47), 105 (37), 95 (100), 93 (59), 91 (46), 81 (55), 79 (47), 67 (66), 55 (60), and 43 (95); for NMR see Table 1.

The Hypoiodite Reaction of 3β,20β-Dihydroxy-12α,17β-ethyletiojervan-11-one 3-Acetate ***17***. Alcohol **17** (267 mg) in dry benzene (40 ml) containing mercury(II) oxide (550 mg) and iodine (850 mg) was irradiated with a 100-W high pressure mercury arc through a Pyrex filter under an argon atmosphere. The solution was stirred during irradiation. The irradiation was discontinued after 2.5 h when the starting material disappeared as shown by TLC. The precipitates

were removed by filtration and washed with hot benzene (100 ml×2). The filtrate and the washings were combined and washed with 10% sodium hydrogen sulfite solution (30 ml) and then with water and dried over anhydrous sodium sulfate. Evaporation of the solvent left a residue (308 mg) which was subjected to column chromatography (Mallincrodt silicic acid, 2.6 g). Elution with a 1:1 mixture of hexane and benzene gave a fraction (10 mg); further elution with benzene, a 2:1 mixture of benzene and chloroform, and a 1:1 mixture of benzene and chloroform gave acetate **19** (216 mg). (Found: *m/e* 374.2438. Calcd for $C_{23}H_{34}O_4$: M^+ 374.2455); IR ($CHCl_3$) 1732 (OAc and 5-membered ring ketone), 1240, 1028, and 758 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*) 374 (M^+, 67.8), 359 (M^+-CH_3, 3.6), 314 ($M^+-CH_3CO_2H$, 9.9), 299 ($M^+-CH_3CO_2H-CH_3$, 12.9), 235 (7.7), 147 (26.7), 105 (25.1), 95 (35.0), 93 (30.7), 91 (29.0), 79 (33.3), 67 (25.1), 55 (19.7), and 43 (100).

The final fraction (19 mg) eluted with a 1:1 mixture of chloroform and diethyl ether was the starting material. Acetate **19** was subjected to hydrolysis without further purification.

Hydrolysis of Acetate ***19***. Acetate **19** (560 mg) in methanol containing potassium hydroxide (2.5 g), water (0.5 ml), and chloroform (8 ml) was stirred for 2.5 h at room temperature and then warmed for another 0.5 h (bath temp 40 °C). The solvent was removed by a rotary evaporator and the residue in added water (30 ml) was neutralized with 2 mol dm^{-3} hydrochloric acid (*ca.* 50 ml) and extracted with chloroform (100 ml×3). The chloroform solution was washed with water and dried over anhydrous sodium sulfate. The residue (532 mg) was recrystallized from diethyl ether to yield 3β-hydroxy-12β-ketone **20**. Preparative TLC of the residue from the filtrate with a 1:1 mixture of diethyl ether and benzene gave a further amount of ketone **20** (27 mg), mp 229—229.5 °C. (Found: *m/e* 332.2352. Calcd for $C_{21}H_{32}O_3$. M^+ 332.2351); $[\alpha]_D^{25}-4$ (*c* 1.4, $CHCl_3$); IR 3410 (OH), 1724 (5-membered ring ketone), 1080, and 1041 cm^{-1}; MS, (70 eV), *m/e* (*rel intensity*) 332 (M^+, 100), 317 (M^+-CH_3, 6.2), 302 (M^+-2CH_3, 26.1), 147 (17.9), 110 (17.7), 109 (13.3), 107 (16.9), 105 (24.0), 97 (28.6), 96 (30.9), 93 (30.3), 91 (30.3), 79 (49.2), 67 (24.9), 55 (25.1), 43 (16.7), and 41 (25.0).

Oxidation of 3β-Hydroxy-12β-ketone with Chromium Trioxide–Pyridine. The 3β-ol **20** (150 mg) and chromium trioxide (150 mg) in pyridine (3 ml) were stirred for 3.5 h at room temperature. To this solution was added more (100 mg) of chromium trioxide in pyridine (1 ml) and the solution was stirred for another 1.5 h. After an excess of chromium trioxide was decomposed by adding saturated sodium hydrogensulfite solution (20 ml), the solution was extracted with chloroform (30 ml×3). The chloroform solution was worked up as usual. A product was recrystallized from acetone to yield 3,11-dione **21**, mp 127—129 °C. (Found: *m/e* 330.2193. Calcd for $C_{21}H_{30}O_3$. M^+ 330.2193); IR, 1706 (6-membered ring ketone), 1728 (5-membered ring, ketone), 1258, 1129, 1084, and 861 cm^{-1}; MS, (70 eV), *m/e* (*rel intensity*), 330 (M^+, 100), 315 (M^+-CH_3, 9.8), 300 (M^+-2CH_3, 37.5), 286 (11.5), 245 (24.2), 191 (18.5), 121 (17.4), 97 (38.3), 96 (42.0), 93 (31.0), 91 (22.5), 81 (21.0), 79 (44.6), 67(20.1), 55 (25.7), 43 (20.9), and 41 (22.9).

Wolff-Kishner Reduction of Ketone ***20***. Ketone **20** (102 mg), hydrazine hydrate (1 ml), and hydrazine hydrochloride (280 mg) in triethylene glycol (7.2 ml) were heated at 130 °C for 4 h under an atmosphere of nitrogen. To this solution was added potassium hydroxide pellets (370 mg) and the solution was distilled until the temperature rose to 210 °C. The solution was heated at that temperature for another 2.5 h (bath temp 223 °C). After cooling, the solution was poured into a water–ice mixture. Crude 11-deoxo compound **22**, (78 mg), mp 158—165 °C, was collected by filtration. The specimen for analysis, mp 171—174 °C, was obtained by recrystallization from acetone–diethyl ether. (Found: C, 78.71; H, 10.72%. Calcd for $C_{21}H_{34}O_2$. C, 79.19; H, 10.76%); IR, 3400 (OH), 1084, and 1049 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*) 318 (M^+, 45.6), 303 (M^+-CH_3, 47.6), 300 (M^+-H_2O, 11.8), 285 (32.7), 274 (11.2), 259 (71.1), 241 (43.7), 149 (72.6), 148 (100), 147 (37.6), 107 (76.1), 105 (48.9), 95 (44.1), 93 (81.1), 91 (77.0), 81 (70.0), 79 (80.6), 67 (71.6), 55 (66.8), 43 (39.4), and 41 (62.1), for NMR see Table 1.

The 3-acetate **23**, mp 135—137 °C, was prepared in a usual manner. (Found: C, 76.68; H, 10.10%. Calcd for $C_{26}H_{36}O_3$: C, 76.62; H, 10.07%. (Found: *m/e* 360.2654. Calcd for $C_{26}H_{36}O_3$. M^+, 360.2664); IR, ($CHCl_3$) 1732 (OAc), 1243, 1087, 1031, and 762 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*) 360 (M^+, 10.5), 345 (19.2), 300 (100), 285 (45.1), 256 (23.9), 255 (23.3), 241 (80.8), 149 (39.0), 148 (53.0), 147 (33.0), 107 (47.0), 105 (33.9), 93 (51.5), 91 (40.6), 81 (40.9), 79 (43.8), 67 (36.7), 55 (32.9), and 43 (93.0).

Preparation of the γ-Lactone ***24*** *from Acetate* ***23*** *with Chromium Trioxide–Acetic Acid.* To a solution of acetate **23** (74 mg) in glacial acetic acid (8.5 ml), under reflux, was added chromium trioxide (234 mg) dissolved in glacial acetic acid (4.5 ml) and water (0.5 ml). The solution was heated under reflux for 2.5 h. After removal of the solvent at below 70 °C, the residue was extracted with chloroform (50 ml×3). The chloroform solution was worked up as usual to yield amorphous γ-lactone **24** (30 mg). All attempts to induce the lactone to become crystals were unsuccessful. (Found: *m/e* 314.2248. Calcd for $C_{21}H_{30}O_2$ ($M^+-CH_3CO_2H$ 314.2245). IR, 1729 (OAc), 1765 (γ-lactone), 1258, and 1023 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*) 374 (M^+, 0.3), 314 (100), and 299 (35.7); for NMR see Table 1.

Hydrolysis of the γ-Lactone ***24*** *with Hydrochloric Acid.* The γ-lactone **24** (40 mg) in methanol (8.1 ml) and chloroform (0.9 ml) containing 12 mol dm^{-3} hydrochloric acid (0.9 ml) was stirred for 17 h at room temperature. The solution was neutralized with aq 5% sodium carbonate solution and the solvent was partly removed by a rotary evaporator. The crystals of the 3β-hydroxy γ-lactone **25** were collected by filtration and recrystallized from methanol–water to yield **25**, mp 202—205 °C. (Found: *m/e* 332.2340. Calcd for $C_{21}H_{32}O_3$: M^+ 332.2350); IR 3400 (OH) and 1765 cm^{-1} (γ-lactone); MS, *m/e* (70 eV) (*rel intensity*) 332 (M^+, 27.4), 314 (M^+-H_2O, 95.8), 299 (22.2), 285 (10.2), 260 (45.1), 259 (30.2), 258 (100), 149 (12.8), 147 (25.5), 108 (14.3), 93 (23.7), 91 (24.6), 79 (24.3), 55 (22.1), and 41 (14.3).

Reduction of Ketone ***19*** *with Lithium Aluminum Hydride.* To 12α-ketone **19** (522 mg) in dry THF (30 ml) cooled by ice–water was added slowly lithium aluminum hydride (400 mg). The solution was stirred for 1.5 h at room temperature and an excess of lithium aluminum hydride was decomposed by addition of small amounts of ethyl acetate and methanol. To this solution were added water (50 ml) and chloroform (100 ml) and the two-layered solution was stirred for 30 min. The solution was filtered and the aqueous filtrate was extracted with chloroform (50 ml×20). The chloroform solution was worked up in the usual manner. The product was recrystallized from diethyl ether to yield **26** (241 mg), mp 211—214 °C. A residue (185 mg) from the filtrate was subjected to preparative TLC with a 1:1 mixture of chloroform–diethyl ether to yield a further amount of diol **26** (26 mg). (Found: M^+ *m/e* 334.2505. Calcd for

$C_{21}H_{34}O_3$: M^+ 334.2506); $[\alpha]_D^{25}$ −3.0 (*c* 0.75, $CHCl_3$); IR, 3428 (OH), 1040, and 851 cm^{-1}; MS, (70 eV) *m/e* (*rel intensity*) 334 (M^+, 6.6), 316 (M^+-H_2O, 100), 301 ($M^+-H_2O-CH_3$, 47.3), 298 (M^+-2H_2O, 10.6), 290 (41.0), 283 (34.6), 147 (66.6), 133 (33.0), 121 (37.6), 119 (37.1), 109 (36.7), 107 (76.8), 105 (66.6), 97 (37.4), 96 (41.1), 95 (77.2), 93 (94.0), 91 (78.1), 81 (75.1), 79 (95.3), 67 (80.7), 55 (80.8), 43 (71.3), and 41 (70.7).

The diol **26** (13 mg) and acetic anhydride (5 mg) in pyridine (0.5 ml) were stirred for 20 h at room temperature. At the time intervals of 1.5 h and 5 h, a more acetic anhydride (0.05 ml) was added. Work-up of the reaction mixture in the usual manner gave a product (13 mg), which was recrystallized from methanol to yield **27**, mp 170—171 °C. (Found: *m/e* 376.2612. Calcd for $C_{23}H_{36}O_4$: M^+ 376.2612), IR, 3490 (OH), 1734 (OAc), and 1242 cm^{-1}; MS *m/e* (*rel intensity*) 376 (M^+, 2.6), 358 (M^+-H_2O, 69.4), 343 (15.8), 316 ($M^+-CH_3CO_2H$, 18.6), 298 ($M^+-CH_3CO_2H-H_2O$, 35.2), 283 (39.9), 147 (43.8), 107 (60.9), 105 (40.0), 95 (55.8), 93 (69.2), 91 (43.9), 81 (55.9), 79 (61.8), 67 (42.5), 55 (38.1), and 43 (100%).

Oppenauer Oxidation of Alcohol ***26***. Alcohol **26** (288 mg) and aluminum isopropoxide (120 mg) in toluene (25 ml) and dry cyclohexanone (2.3 ml) were heated for 1 h under reflux (bath temp 120 °C). More aluminum isopropoxide (140 mg) was added to the solution. The mixture was heated under reflux for another 1 h and then subjected to a steam distillation to give 150 ml of a distillate. To the solution there were added chloroform (50 ml) and water; then the solution was stirred for 1 h. The aqueous layer was again extracted with chloroform. The combined chloroform solution was worked up as usual. The residue (260 mg) was recrystallized from acetone to yield ketone **28** (69 mg), mp 151—152 °C. The filtrate was evaporated and the residue (143 mg) was subjected to column chromatography (Mallincrodt silicic acid, 2.0 g). Elution with a mixture of a 2:1 benzene and hexane gave fraction (120 mg), which was recrystallized from acetone to yield more **28** (16 mg). The residue from the filtrate was subjected to preparative TLC with a 10:1 mixture of chloroform and diethyl ether to yield two fractions. The more mobile fraction gave dione **21** and the less mobile fraction (45 mg) was recrystallized to yield ketone **28** (35 mg), (Found: C, 75.81; H, 97.0%. Calcd for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70%), $[\alpha]_D^{25}$ −2.0 (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3416 (OH), and 1707 cm^{-1} (carbonyl); MS, (80 eV) *m/e* (*rel intensity*) 332 (M^+, 15), 314 (M^+-H_2O, 70), 299 (32), 288 (48), 95 (82), 93 (78), 91 (65), 79 (85), 67 (70), 55 (95), 43 (100), and 41 (78); for NMR see Table 1.

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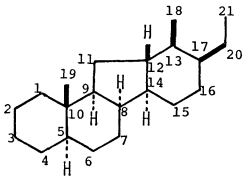

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