12,13-Epoxy-*C*-nor-*D*-homosteroids. VI.[1] Reaction of 17-Oxygenated 12,13-Epoxyetiojervanes with Boron Trifluoride Etherate[2]

Akio MURAI, Noriaki IWASA, Masami TAKEDA, and Tadashi MASAMUNE*

Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060

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17-Oxygenated 12,13-epoxyetiojerv-5-en-3-one 3,3-ethylene acetals (**1A**—**10A**) were treated with boron trifluoride etherate in benzene at room temperature. The epoxy ring cleavage reactions proceeded slowly with increase of electronegativity of the 17-substituents without and/or with deacetalization to give a variety of compounds including rearranged products (**23A** and **23B**). The results summarized in Table 1 indicated that the reactions produced compounds formed by initial cleavage at less electronegative C-12 rather than at C-13 except several compounds (**11A**, **20A**, **20B**, and **34A**). Formation of the latter compounds was attributed by hydride shift or neighboring participation of the 17-acetoxyl groups.

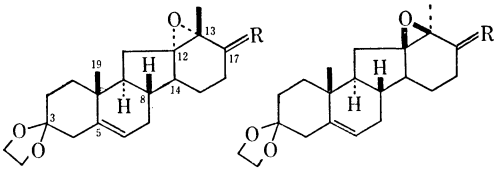
In a previous paper[3] we reported the synthesis and stereochemistry of 17-oxygenated 12,13-epoxyetiojervanes. As a continuing study on the reactions of 12,13-epoxy-*C*-nor-*D*-homosteroids, involving formation of novel rearranged products,[4] we have examined reactions of 17-oxygenated 12α,13α- and 12β,13β-epoxyetiojervanes with boron trifluoride etherate, keeping in mind that the epoxy ring cleavage of the 11-oxygenated 12,13-epoxides varied, depending on electronegativity of the 11-substituents rather than conformation of the epoxy groups.[4] In this paper we describe the results, including interesting participation of neighboring groups.

The reactions of 17α-hydroxy-[3] (**1A**), 17α-acetoxy-[3] (**2A**), 17β-hydroxy-[3] (**3A**), 17β-acetoxy-[3] (**4A**), and 17-oxo derivatives of 12α,13α-epoxyetiojerv-5-en-3-one 3,3-ethylene acetals[3] (**5A**), and the corresponding 12β, 13β-epoxides[3] (**6A**—**10A**) with boron trifluoride etherate were carried out in benzene at room temperature, and the results are summarized in Table 1. The structure of each product was assigned on the basis of the chemical and spectral evidence. The functional groups in the A and B rings, Δ^5-3,3-ethylenedioxy ($S=S_A$) and Δ^4-3-oxo groups ($S=S_B$), the latter being formed by deacetalization of the former under the acidic conditions, were defined clearly on the spectral grounds: (i) S_A, δ ≈3.94 (4H, s, $OC\underline{H}_2C\underline{H}_2O$) and ≈5.40 (1H, br, W_H=8 Hz, 6-H): S_B, λ_{max} 235 nm (ε ≈10000); ν_{max} ≈1660 and ≈1615 cm^{-1}; δ ≈5.78 (1H, s, 4-H), and (ii) difference in chemical shift of 19-methyl protons of several pairs of compounds differing only in these functional groups, $\Delta\delta_{obsd}$ 0.14—0.18; $\Delta\delta_{calcd}$ 0.16.[5]

Table 1. Reaction results of 17-oxygenated 12α,13α-epoxy- (**1A**—**5A**) and 12β,13β-epoxy-13-epietiojerv-5-en-3-one 3,3-ethylene acetals (**6A**—**10A**) with boron trifluoride etherate[a]

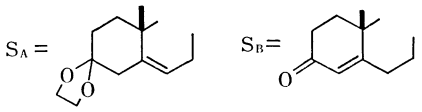
Epoxide	Reaction time	Products (yield/%)[b]
1A	30 s	**11A** (30), **12A** (10), **17A** (5)
2A	30 s	**17A** (16), **17B** (19), **18A** (6)
3A	30 s	**19A** (60), **19B** (22)
4A	20 min	**20A** (34), **20B** (40)
5A	1 h	**5B** (25), **23A** (5), **23B** (25), **24B** (15)
6A	30 s	**25A** (45), **25B** (25), **30A** (15), **30B** (4)
7A	30 s	**26A** (51), **26B** (20)
8A	30 s	**31A** (33), **31B** (28), **32A** (20)
9A	1 min	**34A** (16), **35A** (25)
10A	20 min	**28B** (80)

a) Carried out in benzene at room temperature. b) Isolated yields.



1A R=···OH, −H
2A R=···OAc, −H
3A R=−OH, ···H
4A R=−OAc, ···H
5A R=O

6A R=−OH, ···H
7A R=−OAc, ···H
8A R=···OH, −H
9A R=···OAc, −H
10A R=O



Compound **11A**, mp 132—134 °C, a major product of **1A**, had a molecular formula $C_{21}H_{28}O_3$ corresponding to a dehydration product of **1A**. The IR (ν_{max} 1720 cm^{-1}) and NMR spectra [δ 1.21 (3H, d, J=7 Hz, 18-H)] suggested the presence of a $\Delta^{12(14)}$-17-carbonyl moiety on the six-membered *D* ring. Indeed, compound **11A**, when treated with base (KOH in aq CH_3OH, room temp, 1 h), was converted quantitatively into a known compound, etiojerva-5,12-diene-3,17-dione ethylene acetal[3] (**12A**). The configuration of the 13-methyl group was deduced from the negative Cotton effect (a=+15°) as illustrated in Fig. 1. All these facts establishes that the compound is represented by formula **11A**. The deshielding effect ($\Delta\delta$ 0.12) of a double bond at C-12–C-14 to the chemical shift of the 19-methyl protons [δ_{obsd} 1.10 for **11A**; δ_{calcd} 0.98 and 1.03 for 12β- and 12α-etiojerv-4-en-3-one ethylene acetals[5] (**13A** and **14A**)] was in good accord with the corresponding difference (0.11) between 12β,13α-dihydroacetyljervine[6] (**15**) (δ 1.02) and "diacetyl-Δ^{13}-jervine"[6,7] (**16**) (δ 1.13).

The structure of compound **17A** ($C_{21}H_{26}O_2$), mp 116—118 °C, was based on the spectral data, which gave indications of an aromatic *D* ring: λ_{max} 273 nm

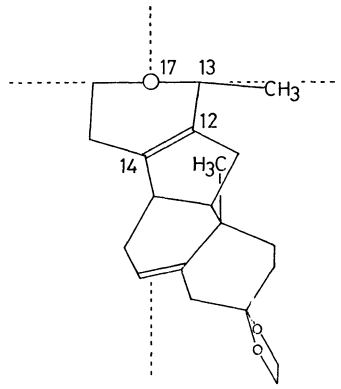
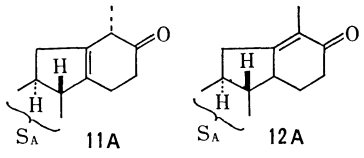


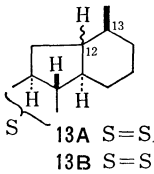
Fig. 1

(ε 300) and 264 (300); δ 2.26 (3H, s, 18-H) and 6.96 (3H, m, W_H=5 Hz, 15-, 16-, and 17-H). The compound (**17A**), on treatment with acid (p-TsOH in a 3:1 mixture of acetone and water, reflux, 4 h) afforded its deacetalization product, Δ^4-3-ketone (**17B**), mp 129—130 °C, in good yield. Naturally, the chemical shifts (δ 1.16 and 1.30) of 19-methyl protons of **17A** and **17B** coincided with those (δ 1.17 and 1.31) of the related veratramine derivatives,[5,8] indicating the deshielding effect of an aromatic D ring to be $\Delta\delta$ 0.17 [1.16 (δ_{obsd} of **17A**)—0.98 (δ_{calcd} of **13A**) or 1.30 (δ_{obsd} of **17B**)—1.14 (δ_{calcd} of **13B**)].

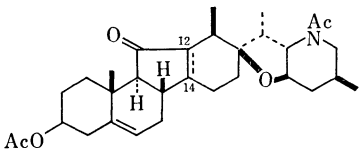


11A

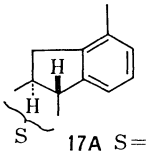
12A



13A S=SA, 12βH
13B S=SB, 12βH
14A S=SA, 12αH

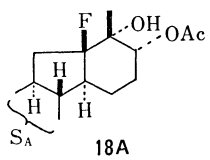


15 12βH, 14αH
16 $\Delta^{12(14)}$

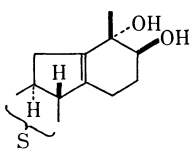


17A S=SA
17B S=SB

The reaction of 17α-acetoxy-12α,13α-epoxide (**2A**) afforded fluorohydrin (**18A**), mp 186—189 °C, as a minor product besides the two aromatic compounds (**17A** and **17B**). The molecular formula $C_{23}H_{33}O_5F$ suggested that **18A** would be a compound formed by simple cleavage of the epoxy ring by a fluoride anion.[9] A 12β-fluoro-13α-hydroxyetiojervane formula (**18A**) was assigned to the compound by analogy of the NMR spectra of the related compounds: 13β-fluoro-12α-hydroxyetiojervanes[10] and the corresponding *C*-nor-*D*-homospirostanes[10,11] exhibited three-proton singlets due to the 18-methyl protons at δ 1.47—1.58, while 12β-fluoro-13α-hydroxyetiojervane,[12] the corresponding spirostan,[11,12] and the relevant compound (**18A**) displayed the singlets at higher fields, δ 1.27, 1.29, and 1.25, respectively.



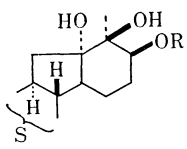
18A



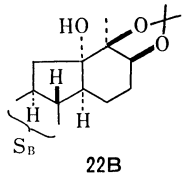
19A S=SA
19B S=SB

Compound **19A**, mp 201—203 °C, obtained as a major reaction product of 17β-hydroxy-12α,13α-epoxide (**3A**), had the same molecular formula $C_{21}H_{30}O_4$ as **3A**. The NMR spectrum revealed a broad singlet (1H, W_H=7 Hz) due to a proton on the carbon (probably C-17) bearing an axial secondary hydroxyl group at δ 3.93 and two singlets (each 3H) due to the 19- and 18-methyl protons at δ 1.08 and 1.35, respectively. In view of the absence of evidence supporting any skeletal rearrangement (no absorption maxima in the carbonyl region), the appearance of the 19- and 18-methyl protons at such low fields indicated the presence of the afore-mentioned double bond at C-12–C-14 (δ_{calcd} 1.10[5] for 19-H). Hence the remaining oxygen atom would have to constitute a tertiary hydroxyl group most probably at C-13. Since the compound did not form the acetonide under the conditions described later, it was formulated as structure **19A**. On the other hand, a minor product, mp 174—177 °C, was readily assigned the corresponding Δ^4-3-ketone formula (**19B**) from the spectral data (Experimental).

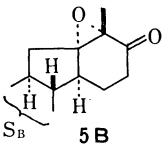
The acid treatment of 17β-acetoxy-12α,13α-epoxide (**4A**) gave two compounds (**20A** and **20B**) as major products. The former (**20A**), mp 204—206 °C, had a molecular formula $C_{23}H_{34}O_6$ corresponding to a hydration product of **4A**, suggesting formation of two new hydroxyl groups. Compound **20A**, formulated as monoacetate [δ 2.06 (3H, s, OCOCH$_3$) and 5.00 (1H, br, W_H=9 Hz, 17-H)], resisted mild acetylation and oxidation with periodic acid. Hydrolysis of **20A** with base (K_2CO_3 in aq CH_3OH, room temp, 3 h) gave triol (**21A**), mp 197—199 °C [δ 3.82 (1H, br, W_H=10 Hz, 17-H)], in 80% yield, which on treatment with acetone and acid ($HClO_4$, room temp, 4 h) underwent acetonide formation with concomitant deacetalization, giving Δ^4-3-oxo triol 13β,17β-acetonide (**22B**), amorphous, in 70% yield [δ 1.44 (9H, s, 18-H and acetonide CH$_3$) and 4.19 (1H, m, W_H=12 Hz,



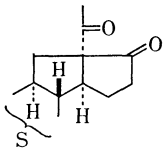
20A S=SA, R=Ac
20B S=SB, R=Ac
21A S=SA, R=H
21B S=SB, R=H



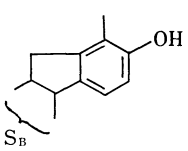
22B



5B



23A S=SA
23B S=SB

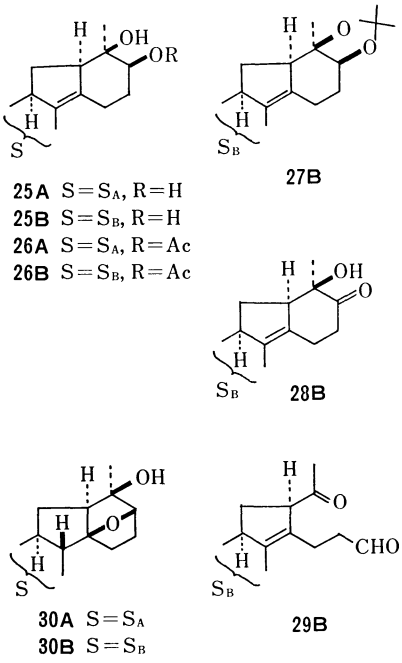


24B

17-H)]. All these facts indicate that the compound is represented favorably by formula **20A**. The latter compound (**20B**), mp 182—184 °C, was also formulated as monoacetate [δ 2.07 (3H, s, $OCOCH_3$) and 5.01 (1H, br, W_H=9 Hz, 17-H)] and was converted under the afore-mentioned basic conditions into triol (**21B**), mp 217—218 °C, in 90% yield, which formed the corresponding acetonide by the same treatment as **21A** in 80% yield. This acetonide was identical with that (**22B**) derived from **20B**, and hence formula **20B** was assigned to the compound. The β-configurational assignment to the 13-hydroxyl group in **20A** and **20B** was understood reasonably by neighboring participation[13] of the *trans*-17β-acetoxyl group adjacent to the relevant α-epoxy group, as discussed later.

Prolonged treatment of 17-oxo-12α,13α-epoxide (**5A**) with the acid produced four compounds. The first compound (**5B**), mp 185—187 °C, was identified easily as a deacetalization product of **5A** by comparison of the spectral data. The second (**23A**), mp 124—125 °C, had the same molecular formula $C_{21}H_{28}O_4$ as **5A**. The spectra revealed that acetyl [ν_{max} 1715 cm^{-1}; δ 2.20 (3H, s)] and five-membered ring carbonyl groups (ν_{max} 1734 cm^{-1}) were newly formed, suggesting cleavage of the C-12–O bond and contraction of the D ring. These data, combined with analogous examples,[4,11] led to assignment of formula **23A** to the compound. The configuration of the acetyl group was deduced from recently reported mechanism on rearrangement of epoxy ketones,[14] as discussed later. The third compound (**23B**), mp 112—113 °C, was identified as a deacetalization product of **23A** on the spectral ground. The fourth compound, mp 289—291 °C, was assigned formula **24B** on the basis of the spectral data indicating the presence of a phenol ring: λ_{max} 285 nm (sh) (ε 900) and 279 (1100); δ 2.15 (3H, s, 18-H), and 6.58 and 6.79 (each 1H, ABq, J=8 Hz, 16- and 15-H).

One (**25A**), mp 102—104 °C, of two major products in the reaction of 17β-hydroxy-12β,13β-epoxide (**6A**) had the same molecular formula as **6A** and gave its monoacetate (**26A**), mp 232—234 °C. The IR and NMR spectra of **25A** and **26A** revealed the presence of secondary (equatorial) and tertiary hydroxyl groups at C-17 and C-13, respectively: **25A**, δ 1.23 (3H, s, 18-H) and 3.41 (1H, br m, W_H=25 Hz, 17-H): **26A**, ν_{max} 3507, 1719, and 1260 cm^{-1}; δ 1.13 (3H, s, 18-H) and 4.77 (1H, do d, J=10 and 5 Hz, 17-H). Compound **25A**, when treated with acid (*p*-TsOH in aq acetone, reflux, 2 h), underwent deacetalization to give another major product (**25B**), mp 185—187 °C, in 80% yield, which also formed its monoacetate (**26B**), mp 123—124 °C. Further treatment of **25B** with acetone and acid ($HClO_4$, room temp, 0.5 h) afforded the corresponding 13β,17β-acetonide (**27B**), oily, though in low yield: δ 1.33 and 1.40 (each 3H, s, acetonide CH_3), and 4.14 (1H, br m, 17-H). Mild oxidation of **25B** with chromium(VI) oxide in pyridine afforded the corresponding 17-ketone (**28B**), mp 178—180 °C, in low yield together with a major product, amorphous, assigned tentatively formula **29B** on the spectral ground (Experimental): **28B**, ν_{max} 3370 and 1717 cm^{-1}. All these facts indicated the presence of 13β- and 17β-hydroxylgroups in **25A** and **25B**. Contrary to the expectation that the remaining double bond would be located at C-12–C-14 as in the case of **19A**, the 19-methyl protons of **25A** and **26A** appeared at abnormally high fields, δ 0.91 and 0.92, compared with those of other usual etiojervanes: δ_{obsd} 1.04, 1.10, 1.08, and 1.02 for **6A**, **11A**, **19A**, and **18A**; δ_{calcd} 0.98 and 1.03 for **13A** and **14A**. The chemical shifts in question were consistent with disposition of a double bond at C-8–C-14, since the shielding effect ($\Delta\delta$ −0.12= 0.91–1.03) of a $\Delta^{8(14)}$-system to the relevant chemical shift has been demonstrated for normal[15] ($\Delta\delta$ 0.117) and *C*-nor-*D*-homosteroids.[11] It is also emphasized that the absorption maximum due to the double bond in question was observed at 208 nm (ε 10000).[16] Hence the compound is represented reasonably by formula **25A**, in which the configuration at C-12 was assigned from the mechanistic ground (hydride shift from C-14 as well as by analogy of the related reactions,[11] as discussed later).

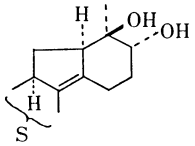


Two minor products, **30A**, mp 207—208 °C, and its deacetalization product (**30B**), mp 136—138 °C, were assigned hydroxy oxolane structures. The former (**30A**), with the same molecular formula $C_{21}H_{30}O_4$ as **6A**, resisted acetylation and oxidation with periodic acid under the usual conditions. While the spectra revealed the presence of a $-CH_3(C)(OH)-$ moiety, in which (C) denotes a quaternary carbon [*m/e* 346 (M^+), 331, and 328; ν_{max} 3580 cm^{-1}; δ 1.30 (3H, s, 18-H)], a one-proton doublet (J=5 Hz) was observed at a relatively low field, δ 4.06. This signal could be ascribed to a proton on the carbon (probably C-17) bearing an ether oxygen atom because of the absence of absorption maxima at 205—210 nm and also at the carbonyl region in the UV and IR spectra. In view of the splitting pattern of the 17-proton (*cf.*, W_H=25 Hz for 17-H of **25A**), the *D*-ring would be deformed considerably and the 17-oxygen atom would constitute an ether bond between C-17 and either one of C-12, C-14, and C-8. The formation of an

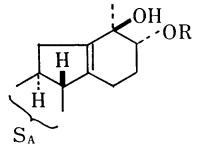
oxetane or an oxane ring (C-12 or C-8) would be eliminated by examination of the Dreiding model and also by inertness to hydride reduction of **30A** ($LiAlH_4$ in THF–dioxane, reflux, 4 h).[17] The compound is therefore be represented favorably by formula **30A**. In view of the fact that interconversion between **25A** and **30A** did not take place under the acidic conditions, compound **30A** would presumably be formed by cleavage of the C-12–O bond, hydride shift of the 14α-hydrogen to C-12, and subsequent intramolecular attack of the 17β-hydroxyl group to the relevant 14-carbenium ion.

Two reaction products of 17β-acetoxy-12β,13β-epoxide (**7A**) were identified as the above-described $\Delta^{8(14)}$-13β,17β-diol 17-acetate (**26A**) and its deacetalization compound (**26B**), respectively, by direct comparison. Naturally, compounds corresponding to **30A** and **30B** could not be detected.

Two major products, **31A**, mp 174—175 °C, and its deacetalization product (**31B**), amorphous, in the reaction of 17α-hydroxy-12β,13β-epoxide (**8A**) were assigned $\Delta^{8(14)}$-13β,17α-diol formulas as follows. The former (**31A**), with the same molecular formula $C_{21}H_{30}O_4$ as **8A**, displayed essentially the same mass and UV spectra as **25A** with the $\Delta^{8(14)}$-13β,17β-dihydroxy moiety: λ_{max} 207 nm (ε 9000). The NMR spectrum also resembled that of **25A**, except a signal due to the 17-proton [δ 3.70 (1H, br, W_H=8 Hz)], indicating that **31A** differed from **25A** only in configuration of the 17-hydroxyl group. The same situation held for the relation between **31B** and **25B**. Indeed, compound **31B**, when oxidized with chromium(VI) oxide in pyridine (room temp, 0.6 h) afforded the afore-mentioned hydroxy ketone (**28B**), mp 178—180 °C, confirming the assigned structures to compounds **31A** and **31B**. A minor product (**32A**), mp 169—171 °C, with the same molecular formula as **8A**, gave its monoacetate (**33A**), mp 119—121 °C, which still showed an absorption maximum at 3440 cm^{-1} due to a hydroxyl group. These facts, coupled with the mass spectrum [**32A**, *m/e* 346 (M^+), 331, 328, 302 (M^+—$CH(OH)CH_2$), and 234], suggested that **32A** would probably possess a partial formula of –(CH_3)(C)(OH)CH(OH)CH_2– on the D ring. However, the UV (no absorption maximum above 205 nm) and NMR spectra [δ 1.12 and 1.29 (each 3H, s, 19- and 18-H)] differed clearly from those of **31A** [δ 0.90 and 1.20 (each 3H, s, 19- and 18-H)]. These spectra were consistent with disposition of a double bond at C-12–C-14: δ_{calcd} 1.10 and 0.91 for 19-H of **32A** and **31A**. Hence the $\Delta^{12(14)}$-13β,17α-diol structure (**32A**) was assigned to the minor compound.



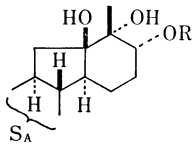
31A S=S_A
31B S=S_B



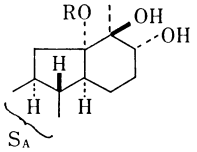
32A R=H
33A R=Ac

The reaction of 17α-acetoxy-12β,13β-epoxide (**9A**) with the acid gave rise to a complex mixture, from which two compounds (**34A** and **35A**) were isolated with a mixture of the respective deacetalization products. The former (**34A**), mp 217—219 °C, had a molecular formula $C_{23}H_{34}O_6$ corresponding to that of a hydration product of **9A**. The NMR spectrum exhibited a three-proton singlet due to 18-methyl protons at δ 1.22 and a broad multiplet (1H, W_H= 17 Hz) due to a proton on the 17-carbon bearing an equatorial acetoxyl group at δ 5.14. Compound **34A**, when hydrolyzed with base (KOH in CH_3OH, room temp, 5 h), yielded triol (**36A**), mp 207.5—208.5 °C, showing no carbonyl band in the IR spectrum. This triol (**36A**), on treatment with acetone and acid under the same conditions as described above, gave Δ^4-3-oxo triol 13α,17α-acetonide (**37B**), amorphous, whose spectra (Experimental) were in good accord with the assigned structure. All these facts, combined with the formation of **20A** from **4A**, led to assignment of formula **34A** to the compound. On the other hand, compound **35A**, amorphous, had the same molecular formula as **34A** and displayed three three-proton singlets at δ 1.02, 1.18, and 2.08 and a broad multiplet (1H, W_H=22 Hz) at δ 3.72, which were attributed to 19-, 18-, acetoxyl methyl protons and a proton at C-17, respectively. The compound (**35A**) was hydrolyzed by base treatment to give triol (**38A**), mp 199.5—201.5 °C [δ 2.60, 2.66, and 2.71 (each 1H, s, 3OH) and 3.68 (1H, br, W_H=14 Hz, and 6 Hz on addition of D_2O, 17-H), which on treatment with acid (*p*-TsOH in aq acetone, reflux, 2 h) gave the corresponding Δ^4-3-ketone (**38B**), mp 197—198 °C. Oxidation of **38B** with chromium(VI) oxide in pyridine afforded 17-ketone (**39B**), mp 171.5—173 °C: ν_{max} 3605, 3510, and 1715 cm^{-1}; δ 1.58 and 3.66 (each 1H, s, 2OH). The same 17-ketone was also obtained by oxidation of **21B** (12α,13β,17β-triol) under the same conditions as that of **38B**, establishing the presence of a 12α,13β,17α-trihydroxy moiety in compound **38B**. These facts, coupled with neighboring participation of the 17α-acetoxyl group, indicated that the compound is represented favorably by formula **35A**.

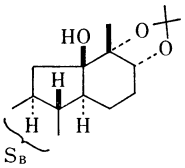
The epoxy cleavage reaction of 17-oxo-12β,13β-epoxide (**10A**) with the acid proceeded rather slowly with concomitant deacetalization to give ketone, mp 178—180 °C, in 80% yield as a sole product, which



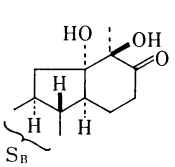
34A R=Ac
36A R=H



35A S=S_A, R=Ac
38A S=S_A, R=H
38B S=S_B, R=H



37B

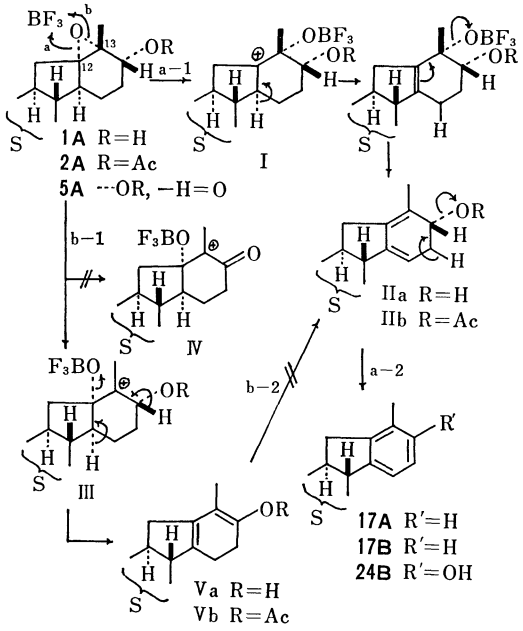


39B

was identified as the afore-mentioned $\Delta^{8(14)}$-13β-hydroxy-17-ketone (**28B**).

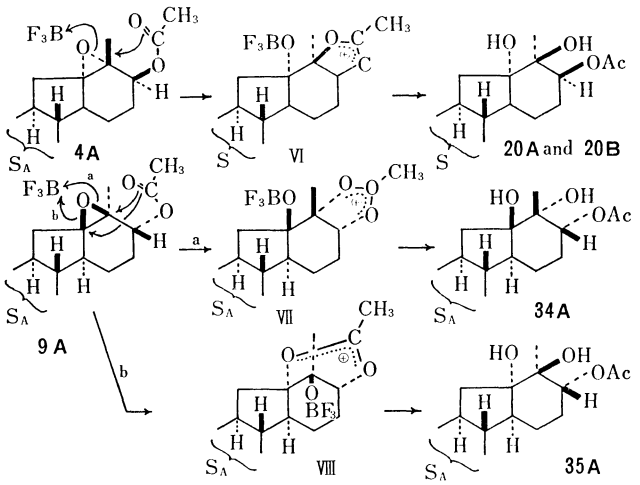
The results in Table 1 are summarized as follows. The reactions gave rise to products resulting from the epoxy ring cleavage at C-12 rather than C-13 for all the starting epoxides (**1A**—**10A**) except those **11A**, **20A**, **20B**, and **34A**. The preferential C-12–O bond cleavage, combined with the previously reported analogous results on acid treatment of 11-oxygenated 17α-aceytl-12,13-epoxides,[4] is understood well by the difference in stability of incipient carbenium ions at C-12 and C-13 formed by the epoxide opening. The fact that the reactions proceeded slowly with increase of electronegativity of the 17-substituents is also in good accord with the preferential cleavage of the C-12–O bond. These results are discussed in more details in the following.

(i) The formation of aromatic compounds (**17A**, **17B**, and **24B**) is rationalized well by assuming the initial cleavage of the C-12–O bond (Scheme 1). The route a (initial cleavage of the C-12–O bond) would give a 12-carbenium ion (I) (step a-1), which would be transformed smoothly *via* diene alcohol (IIa) or its acetate (IIb) into the aromatic compounds (step a-2). The reaction of 17α-acetate (**2A**) leading to the predominant formation of **17A** and **17B**, compared with the formation of **17A** from 17α-alcohol (**1A**) as a minor product, is ascribed to facile removal of the acetoxyl function as a leaving group (step a-2). On the other hand, the route b (initial cleavage of the C-13-O bond) must involve relatively unstable 13-carbenium ions (III) or (IV) (step b-1). Moreover, conversion of dienol (Va) or dienol acetate (Vb), formed from III, into IIa or IIb (step b-2) would not easily proceed under the acidic conditions.



Scheme 1. Pathway for formation of **17A**, **17B**, and **24B**.

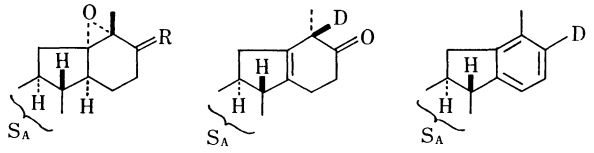
(ii) The reaction results of **4A** and **9A**, in which the 17-acetoxyl groups are oriented *trans* to the 12,13-epoxy groups, are explained reasonably on the basis of participation of the acetoxyl groups to epoxy bond cleavage leading to formation of acetoxonium ion intermediates (VI—VIII) (Scheme 2). While we have a few of analogous precedents[13] regarding the relevant participation controlling epoxy ring opening, the formation of **35A** from **9A** is very noteworthy in the sense that a 1,3-diaxial acetoxonium ion (VIII) is required as an intermediate, resulting from attack of the 17β-acetoxy function to an alternate, not adjacent, epoxy carbon atom (C-12). Moreover, the difference in reactivity between **4A** and **9A** would be attributed to that between conformations of the respective 17-acetoxyl groups, as suggested by the Dreiding model and demonstrated by the NMR spectra (17-H, W_H=6 Hz for **4A** and 14 Hz for **9A**).



Scheme 2. Pathways for formation of **20A**, **34A**, and **35A**.

(iii) The reaction of 17α-hydroxy-12α,13α-epoxide (**1A**). especially the formation of β,γ-unsaturated ketone (**11A**), was examined in more detail. Reduction of 12α,13α-epoxy-17-ketone (**5A**) with sodium borodeuteride (>98%) afforded alcohol-17-*d* (**40A**), mp 169—171 °C, and its 17-epimer (**41A**), mp 154.5—157 °C, in 79 and 20% yields, respectively. These alcohols showed almost the same parent peaks at *m/e* 347 (0.59 and 0.66%) in the mass spectra and the same R_f values on TLC as **1A** and **3A**, respectively. Naturally, these alcohols (**40A** and **41A**) were reconverted by oxidation with chromium(VI) oxide in pyridine into the original ketone (**5A**). Reaction of **40A**, a 17-*d* derivative of **1A**, under the same acidic conditions as that of **1A** resulted in isolation of two deuterated compounds (**42A** and **43A**), mp 133—135 °C and 116—118.5 °C, which were corresponding to **11A** and **17A**, respectively. In accordance with the assigned structures, the former (**42A**) (isotope content, >75% by MS and NMR) exhibited a parent peak at *m/e* 329 (1.73%) and a singlet due to the 18-methyl protons at δ 1.21 in the mass and NMR spectra, while the latter (**43A**) (>98%) displayed a parent peak at *m/e* 311 (2.48%) and an AB type quartet (J=8 Hz) due to the 15- and 16-protons at δ 6.97 and 7.06. Furthermore, compound **42A**, when treated with base under the afore-mentioned conditions, was transformed into the undeuterated α,β-unsaturated ketone (**12A**).

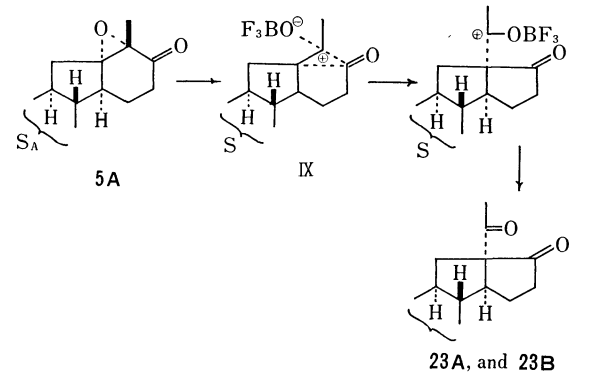
These results established that (i) formation of **11A** resulted from cleavage of the epoxy ring at more electronegative C-13 and hydride shift of the 17β-hydrogen to C-13 in a concerted manner,[18] and (ii) reaction of **1A** to the aromatic compound (**17A**) proceeded *via* route a but not route b (Scheme 1).



40A R=···OH, −D
41A R=−OH, ···D

42A **43A**

(iv) The reaction of 17-oxo-12α,13α-epoxide (**5A**) gave rise to rearranged products (**23A** and **23B**), which evidently resulted from migration of the C-17–C-13 bond (acyl) to C-12 *via* an intermediate (IX) formed by cleavage of the C-12–O bond (Scheme 3). It has been reported that the acyl migration[19] is preferred over a hydrogen or a primary alkyl shift[19b] and occurs in aprotic solvents in a concerted manner with inversion of the configuration at the migration terminus.[14] The configuration of **23A** and **23B** was deduced from these mechanistic grounds. The fact that no rearranged product was obtained in the reaction of 17-oxo-12β,13β-epoxide (**10A**) would probably be ascribed to difficult formation of *trans*-fusion of two five-membered (*C*/*D*) rings.



5A IX **23A**, and **23B**

Scheme 3.

In summary we again emphasize that all the reactions, except those involving the hydride shift and neighboring participation of the acetoxyl groups, were initiated by the epoxy ring cleavage at the less electronegative C-12. It is also noteworthy that the products with a double bond at C-12–C-14 were isolated only from the 12β,13β-epoxides.

Experimental

All the melting points were uncorrected. The homogeneity of each compound was always checked by TLC on silica gel (Wakogel B-5) with various solvent systems, and the spots were developed with cerium(IV) in dil sulfuric acid and/or iodine. Column chromatography was carried out over silica gel (Merck, Kieselgel 60, 70—230 mesh) or over alumina (Merck, Aluminiumoxid G. Type E), and preparative TLC over silica gel (Wakogel B-5F, 20×20 cm^2), unless otherwise stated. The optical rotations, UV, and IR spectra were measured in chloroform, ethanol, and Nujol, respectively, unless otherwise stated. The NMR spectra were obtained in chloroform-*d* at 100 MHz, TMS being used as an internal reference. The abbreviations, "s, d, q, m, br, do, and sh," in the NMR and IR spectra denote "singlet, doublet, quartet, multiplet, broad, double, and shoulder," respectively.

*Reaction of 12α,13α-Epoxy-17α-hydroxyetiojerv-5-en-3-one 3,3-Ethylene Acetal (**1A**) with Boron Trifluoride Etherate (BF_3).* To a benzene solution (100 ml) of **1A** (450 mg) was added rapidly BF_3 (0.2 ml) in benzene (3 ml) under stirring, and the resulting dark-blue solution was stirred at room temperature for 30 s. The reaction was ceased by rapid addition of ether (70 ml) and 5% aq sodium hydrogencarbonate ($NaHCO_3$, 70 ml), when the mixture became yellow. The benzene-ether solution was washed with 5% aq $NaHCO_3$ (3×80 ml) and water (3×100 ml), dried over anhydrous sodium sulfate and evaporated to dryness to leave resinous substance (430 mg), which was separated by chromatography over silica gel (25 g), benzene-ether mixtures being used as solvents. Fractions eluted with benzene-ether (10:1) gave etiojerva-5,12,14,16-tetraen-3-one 3,3-ethylene acetal (**17A**, 25 mg), mp 116—118 °C (from ether) and $[\alpha]_D$ −84.7°; MS, *m/e* 310 (M^+); UV, λ_{max} 273 nm (ε 300), 264 (300), 220 (sh) (5000), 215 (sh) (6300), and 205 (9000); IR, ν_{max} 1108 and 1095 cm^{-1}; NMR, δ 1.16 and 2.26 (each 3H, s, 19- and 18-H), 3.94 (4H, s, $OC_2\underline{H}_4O$), 5.47 (1H, br, W_H=10 Hz, 6-H), and 6.96 (3H, m, W_H=5 Hz, 15-, 16-. and 17-H). Found: C, 80.81; H, 8.57%. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Fractions eluted with benzene-ether (10:2) gave 13-epietiojerva-5,12(14)-diene-3,17-dione 3,3-ethylene acetal (**11A**, 118 mg), mp 132—134 °C (from ether) and $[\alpha]_D$ −55.6°; ORD (dioxane), $[\phi]_{322}^{trough}$ −1540°, $[\phi]_{293}^{peak}$ 0°, and a=+15°, MS, *m/e* 328 (M^+), 313, 300, and 286; IR, ν_{max} 1720, 1113, and 1101 cm^{-1}; NMR, δ 1.10 (3H, s, 19-H), 1.21 (3H, d, J=7 Hz, 18-H), 3.97 (4H, s, $OC_2\underline{H}_4O$), and 5.41 (1H, br, W_H=10 Hz, 6-H). Found: C, 76.49; H, 8.80%. Calcd for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59%. Fractions eluted with benzene-ether (2:1) afforded α,β-unsaturated ketone (22 mg), mp 162—164 °C, which was identical with an authentic sample of etiojerva-5,12-diene-3,17-dione 3,3-ethylene acetal[3] (**12A**) (UV, IR, NMR, and TLC).

Compound **11A** (25 mg) was treated with 5% potassium hydroxide (KOH) in methanol (1 ml) at room temperature for 1 h. After removal of the solvent, the residue was mixed with water and 2M hydrochloric acid (pH≈6) and extracted with chloroform (4×10 ml). The chloroform solution was washed with 5% aq $NaHCO_3$ (2×20 ml) and water (2×20 ml), dried and evaporated to leave amorphous substance (23 mg), showing a single spot, which was purified by preparative TLC (1 plate) over silica gel with benzene-ether (3:1) to yield **12A** (14 mg), which had mp 164—165 °C on trituration with isopropyl ether.

*Reaction of 12α,13α-Epoxy-17α-hydroxyetiojerv-5-en-3-one 17-Acetate 3,3-Ethylene Acetal (**2A**) with BF_3.* A solution of **2A** (250 mg) in benzene (25 ml) was stirred with BF_3 (0.25 ml) at room temperature for 30 s. After addition of ether (50 ml) and 5% aq $NaHCO_3$ (50 ml), the benzene-ether solution was worked up as mentioned above to leave resinous substance, showing several spots on TLC, which was separated into three fractions by chromatography over silica gel (15 g) as usual. Most mobile fractions gave **17A** (32 mg), mp 114—116 °C (from ether). Middle fractions afforded etiojerva-4,12,14,16-tetraen-3-one (**17B**, 27 mg), mp 129—130 °C (from ether) and $[\alpha]_D$ +75.6°; MS, *m/e* 266 (M^+);

UV, λ_{max} 272 nm (ε 300), 237 (8400), and 219 (7600); IR, ν_{max} 1665 and 1613 cm^{-1}; NMR, δ 1.30 and 2.26 (each 3H, s, 19- and 18-H), 5.79 (1H, s, 4-H), and 6.97 (3H, s, W_H= 5 Hz, 15-, 16-, and 17-H). Found: C, 85.79; H, 8.19%. Calcd for $C_{19}H_{22}O$: C, 85.67; H, 8.33%. Least mobile fractions gave 12β-fluoro-13α,17α-dihydroxyetiojerv-5-en-3-one 17-acetate 3,3-ethylene acetal (**18A**, 15 mg), mp 186—189 °C (from ether) and $[\alpha]_D$ −53.0°; MS, *m/e* 408 (M^+), 388 (M^+−HF), and 364; IR, ν_{max} 3500, 1718, 1260, and 1110 cm^{-1}; NMR, δ 1.02, 1.25, and 2.10 (each 3H, s, 19- and 18-H, and OCOCH_3), 3.94 (4H, s, OC_2H_4O), 4.94 (1H, br, W_H=20 Hz, 17-H), and 5.36 (1H, br, W_H=10 Hz, 6-H). Found: C, 67.89; H, 8.16%. Calcd for $C_{23}H_{33}O_5F$: C, 67.62; H, 8.08%.

*Reaction of 12α,13α-Epoxy-17β-hydroxyetiojerv-5-ene-3,17-dione 3,3-Ethylene Acetal (**3A**) with BF_3.* Compound **3A** (110 mg) was treated with BF_3 (0.04 ml) in benzene (27 ml) at room temperature for 30 s under stirring. The reaction mixture was worked up as mentioned above to leave amorphous substance (130 mg), showing two main spots on TLC, which was separated by preparative TLC (6 plates) over silica gel with benzene–ether (1:3). A fraction with higher R_f value gave 13α,17β-dihydroxyetiojerva-5,12(14)-dien-3-one 3,3-ethylene acetal (**19A**, 60 mg), mp 201—203 °C and $[\alpha]_D$ −50.8°; MS, *m/e* 346 (M^+) and 303; IR, ν_{max} 3535, 3380, and 1095 cm^{-1}; NMR, δ 1.08 and 1.35 (each 3H, s, 19- and 18-H); 3.93 (5H, br s, W_H=7 Hz, 17-H and OC_2H_4O), and 5.36 (1H, br, W_H=10 Hz, 6-H). Found: C, 72.95; H, 8.85%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. A fraction with lower R_f value afforded 13α,17β-dihydroxyetiojerva-4,12(14)-dien-3-one (**19B**, 23 mg), mp 174—177 °C (from ether) and $[\alpha]_D$ +57.2°; MS, *m/e* 302 (M^+) and 259; UV, λ_{max} 237 nm (ε 9600); IR, ν_{max} ($CHCl_3$) 3640, 3460, 1662, 1613, 1110, 1010, and 960 cm^{-1}; NMR, δ 1.24 and 1.36 (each 3H, s, 19- and 18-H), 3.96 (1H, br, W_H=7 Hz, 17-H), and 5.75 (1H, s, 4-H). Found: C, 75.38; H, 8.77%. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67%.

*Reaction of 12α,13α-Epoxy-17β-hydroxyetiojerv-5-en-3-one 17-Acetate 3,3-Ethylene Acetal (**4A**) with BF_3.* To a benzene solution (80 ml) of **4A** (320 mg) was added BF_3 (0.2 ml) in benzene (2 ml) under stirring. The resulting dark-green mixture was stirred at room temperature for 20 min. The reaction was ceased by addition of 5% aq $NaHCO_3$ (80 ml), when the mixture became yellow. The benzene solution was worked up as usual to leave resinous substance (320 mg), which was separated into three fractions by chromatography over silica gel (90 g) with benzene–ether mixtures. Initial fractions eluted with benzene–ether (1:1) gave the unreacted epoxide (**4A**, 43 mg). Early fractions eluted with benzene–ether (1:1) afforded 12α,13β,17β-trihydroxy-13-epietiojerv-5-en-3-one 17-acetate 3,3-ethylene acetal (**20A**, 115 mg), mp 204—206 °C (from ether–acetone) and $[\alpha]_D$ −25.4°; MS, *m/e* 406 (M^+), 388, 370, and 346; IR, ν_{max} 3530, 3460, 3350, 1730, 1267, 1105, 1090, and 1020 cm^{-1}; NMR, δ 1.02, 1.20, and 2.06 (each 3H, s, 19- and 18-H, and OCOCH_3), 3.93 (4H, s, OC_2H_4O), 5.00 (1H, br, W_H=9 Hz, 17-H), and 5.34 (1H, br, W_H=10 Hz, 6-H). Found: C, 67.59; H, 8.68%. Calcd for $C_{23}H_{34}O_6$: C, 67.95; H, 8.43%. Later fractions eluted with benzene–ether (1:1) gave 12α,13β,17β-trihydroxy-13-epietiojerv-4-en-3-one 17-acetate (**20B**, 140 mg), mp 182—184 °C (from ether–acetone) and $[\alpha]_D$ +124°; MS, *m/e* 362 (M^+), 344, 302, 284, and 266; UV, λ_{max} 239 nm (ε 9700); IR, ν_{max} 3490, 3400, 1712, 1668, 1610, 1263, and 1024 cm^{-1}; NMR, δ 1.17, 1.20, and 2.07 (each 3H, s, 19- and 18-H, and OCOCH_3), 5.01 (1H, br, W_H=9 Hz, 17-H), and 5.74 (1H, s, 4-H). Found: C, 69.83; H, 8.35%. Calcd for $C_{21}H_{30}O_5$; C, 69.58; H, 8.34%.

Compound **20A** (20 mg) was treated with potassium carbonate (K_2CO_3, 8 mg) in water (2 ml) at room temperature for 3 h under stirring. The reaction mixture was mixed with saturated brine (40 ml) and extracted with chloroform (3×10 ml). The chloroform solution was washed with water (3×20 ml), dried and evaporated to leave amorphous residue, showing a single spot on TLC, which was purified by preparative TLC (1 plate) over silica gel with ether, giving 12α,13β,17β-trihydroxy-13-epietiojerv-5-en-3-one 3,3-ethylene acetal (**21A**, 14 mg), mp 197—199 °C (from acetone) and $[\alpha]_D$ −33.2°; MS, *m/e* 364 (M^+), 346, and 328; IR, ν_{max} 3460, 3360, 1117, 1100, 1023, and 990 cm^{-1}; NMR, δ 1.05 and 1.29 (each 3H, 19- and 18-H), 3.82 (1H, br, W_H=10 Hz, 17-H), 3.94 (3H, s, OC_2H_4O), and 5.37 (1H, br, W_H=10 Hz, 6-H). Found: C, 69.23; H, 8.84%. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85%.

Compound **20B** (20 mg) in methanol (8 ml) was treated with K_2CO_3 (8 mg) in water (2 ml) in the same manner as **20A**. The reaction mixture was worked up as described above to yield 12α,13β,17β-trihydroxy-13-epietiojerv-4-en-3-one (**21B**, 13 mg), mp 217—218 °C (from acetone) and $[\alpha]_D$ +79.4°; MS, *m/e* 320 (M^+), 302, 284, and 266; UV, λ_{max} 239 nm (11000); IR, ν_{max} 3470, 1638, and 990 cm^{-1}; NMR, δ 1.20 and 1.30 (each 3H, s, 19- and 18-H), 3.82 (1H, br, W_H =11 Hz, 17-H), and 5.76 (1H, s, 4-H). Found: C, 70.87; H, 8.88%. Calcd for $C_{19}H_{28}O_4$: C, 71.22; H, 8.81%.

A solution of **21A** (37 mg) in acetone (8 ml) was stirred with 60% aq perchloric acid ($HClO_4$, 0.5 ml) at room temperature for 4 h. The solution was mixed with 5% aq $NaHCO_3$ (2 ml) and saturated brine (2 ml), and extracted with chloroform (4×10 ml). The chloroform extracts were washed with water (3×10 ml), dried and evaporated to yield amorphous residue, which was purified by preparative TLC (2 plates) over silica gel with ether–ethyl acetate (5:1) to give 12α,13β,17β-trihydroxy-13-epietiojerv-4-en-3-one 13β,17β-acetonide (**22B**, 25 mg), showing a single spot, amorphous and $[\alpha]_D$ +88.0 °; MS, *m/e* 360 (M^+), 345, 327, 302 (M^+−C_3H_6O), 284, and 267; UV, λ_{max} 239 nm (ε 12000); IR, ν_{max} ($CHCl_3$) 3580, 3440, 1660, 1615, 1380, 1376, and 1071 cm^{-1}; NMR, δ 1.17 (3H, s, 19-H) and 1.44 (9H, s, 18-H and acetonide CH_3), 4.19 (1H, br, W_H=12 Hz, 17-H), and 5.76 (1H, s, 4-H). Found: C, 72.99; H, 9.39%. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%.

Compound **21B** (8 mg) in acetone (2 ml) was stirred with 60% aq $HClO_4$ (0.1 ml) in the same manner as **21A**. The reaction mixture was worked up as usual to give the amorphous acetonide (7 mg) identical with **22B** (UV, IR, NMR, and TLC).

*Reaction of 12α,13α-Epoxyetiojerv-5-ene-3,17-dione 3,3-Ethylene Acetal (**5A**) with BF_3.* Compound **5A** (400 mg) in benzene (100 ml) was treated with BF_3 (0.36 ml) in benzene (3 ml) at room temperature for 1 h under stirring, when a small spot of **5A** was still detected on TLC. After addition of ether (50 ml) and 5% aq $NaHCO_3$, the mixture was separated into the benzene–ether and aqueous solutions. The former was worked up as usual to a resinous mixture, which was separated and purified by chromatography over silica gel (25 g) with benzene–ether mixtures. Initial two fractions eluted with benzene–ether (6:1) afforded the unchanged epoxide (**5A**, 24 mg) and 13α-acethyl-18,*C*-dinorcholest-5-ene-3,17-dione 3,3-ethylene acetal (**23A**, 20 mg), mp 124—125 °C (from ether) and $[\alpha]_D$ −72.1°; MS, *m/e* 344 (M^+) and 301; IR, ν_{max} 1734, 1715, 1361, and 1105 cm^{-1}; NMR, δ 0.96 and 2.20 (each 3H, s, 19-H and COCH_3), 3.94 (4H, s, OC_2H_4O), and 5.38 (1H, br, W_H=11 Hz, 6-H). Found: C, 73.08; H, 8.31%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%. Next two fractions eluted with benzene–ether (6:

1) gave 17-hydroxyetiojerva-4,12,14,16-tetraen-3-one (**24B**, 60 mg), mp 289—291 °C (from $CHCl_3$) and $[\alpha]_D$ +48.4°, and 12α,13α-epoxyetiojerv-4-ene-3,17-dione (**5B**, 90 mg), mp 185—187 °C and $[\alpha]_D$ +82.9°. **24B**, MS, *m/e* 282 (M^+) and 160; UV, λ_{max} 285 nm (sh) (ε 900), 279 (1100), and 234 (9000); IR ν_{max} 3280, 1648, 1600, and 830 cm^{-1}; NMR, δ 1.28 and 2.15 (each 3H, 19- and 18-H), 5.78 (1H, s, 4-H), 6.58 and 6.79 (each 1H, ABq, J=8 Hz, 16- and 15-H). Found: C, 80.60; H, 7.72%. Calcd for $C_{19}H_{22}O_3$: C, 80.81; H, 7.85%. **5B**, MS, *m/e* 300 (M^+), 285, 257, and 214; UV, λ_{max} 237 nm (ε 9500); IR ν_{max} 1716, 1673, and 1613 cm^{-1}; NMR, δ 1.20 and 1.36 (each 3H, s, 19- and 18-H), and 5.80 (1H, s, 4-H). Found: C, 75.68; H, 8.16%. Calcd for $C_{19}H_{24}O_3$: C, 75.94; H, 8.05%. Fractions eluted with benzene-ether (4:1) afforded 13α-acetyl-*C*,18-dinorcholest-4-ene-3,17-dione (**23B**, 90 mg), mp 112—113 °C (from ether) and $[\alpha]_D$ +74.0°; MS, *m/e* 300 (M^+), 285 and 257, UV, λ_{max} 237 nm (ε 10000), IR, ν_{max} 1733, 1700, 1679, 1615, and 1365 cm^{-1}; NMR, δ 1.14 and 2.20 (each 3H, s, 19-H and $COCH_3$), and 5.73 (1H, s, 4-H). Found: C, 75.82; H, 8.06%. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05%.

*Reaction of 12α,13β-Epoxy-17β-hydroxy-13-epietiojerv-5-en-3-one 3,3-Ethylene Acetal (**6A**) with BF_3.* To a benzene solution (50 ml) of **6A** (200 mg) was added rapidly BF_3 (0.06 ml) in benzene (2 ml) under stirring, and the dark-blue solution was stirred at room temperature for 30 s, when the solution became brown. The reaction was ceased by addition of ether (50 ml) and 5% aq $NaHCO_3$ (50 ml). The benzene-ether solution was worked up as mentioned above to leave amorphous substance, which was separated roughly by chromatography over silica gel (8 g) with a 2:1 mixture of benzene and ether. Early eluates contained two compounds, which were separated by preparative TLC (6 plates) over silica gel with ether to give 14β,17β-epoxy-13β-hydroxy-12α,13-epietiojerv-5-en-3-one 3,3-ethylene acetal (**30A**, 29 mg), mp 207—208 °C and $[\alpha]_D$ −45.2°, and 13β,17β-dihydroxy-12α,13-epietiojerva-5,8(14)-dien-3-one 3,3-ethylene acetal (**25A**, 90 mg), mp 102—104 °C (from ether-hexane) and $[\alpha]_D$ −37.2°. **30A**, MS, *m/e* 346 (M^+), 331, 328, and 303; IR, ν_{max} 3580, 1200, 1140, 1130, 1100, 1080, 1060, 1040, 970, and 940 cm^{-1}; NMR, δ 1.08 and 1.30 (each 3H, s, 19- and 18-H), 3.95 (4H, s, OC_2H_4O), 4.06 (1H, d, J=5 Hz, 17-H), and 5.38 (1H, br, W_H=10 Hz, 6-H). Found: C, 72.84; H, 8.71%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. **25A**, MS, *m/e* 346 (M^+), 331, 328, and 313; UV, λ_{max} 208 nm (ε 10000); IR, ν_{max} 3420, 1095, and 1018 cm^{-1}; NMR, δ 0.91 and 1.23 (each 3H, s, 19- and 18-H), 3.41 (1H, br, W_H= 25 Hz, 17-H), 3.94 (4H, s, OC_2H_4O), and 5.34 (1H, br, W_H=8 Hz, 6-H). Found: C, 73.15; H, 8.32%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. Later eluates also consisted of at least two compounds, from which the following were isolated by preparative TLC (3 plates over silica gel with ether. 13β,17β-Dihydroxy-12α,13-epietiojerva-4,8(14)-dien-3-one (**25B**, 49 mg), mp 185—187 °C and $[\alpha]_D$ +83.3°; MS, *m/e* 302 (M^+) and 284; UV, λ_{max} 234 nm (ε 12000) and 208 (10000); IR, ν_{max} 3530, 3380, 1650, 1618, 1120, 1060, and 1002 cm^{-1}; NMR, δ 1.07 and 1.24 (each 3H, s, 19- and 18-H), 3.45 (1H, br, W_H=22 Hz, 17-H), and 5.82 (1H, s, 4-H). Found: C, 74.99; H, 8.57%. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67%. 14β,17β-Epoxy-13β-hydroxy-12α,13-epietiojerv-5-en-3-one (**30B**, 13 mg), mp 136—138 °C (from ether-hexane) and $[\alpha]_D$ +60.2°; MS, *m/e* 302(M^+), 287, 284, and 259; UV, λ_{max} 237 nm (ε 11000); IR, ν_{max} 3460, 1660, 1610, 1010, 990, 952, and 912 cm^{-1}; NMR, δ 1.23 and 1.31 (each 3H, s, 19- and 18-H), 4.07 (1H, d, J=5 Hz, 17-H), and 5.75 (1H, s, 4-H). Found: C, 75.81; H, 8.60%. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67%.

Compounds **25A** (12 mg) and **25B** (12 mg) were treated with acetic anhydride (0.6 ml) and pyridine (0.12 ml) at room temperature for 20 h under stirring. The respective reaction mixtures were mixed with cold water (5 ml) and extracted with chloroform (3×10 ml). The extracts were washed with 5% aq $NaHCO_3$ to give the corresponding monoacetates (**26A**, 9 mg, and **26B**, 10 mg), which were identical with the reaction products of **7A** described later.

Compound **25A** (42 mg) was refluxed with *p*-toluenesulfonic acid (*p*-TsOH, 22 mg) in acetone (13 ml) and water (2 ml) for 2 h under stirring. The mixture was evaporated to leave amorphous residue, which was treated with 5% aq $NaHCO_3$ and chloroform. The chloroform extracts were worked up as usual to leave crystalline residue (41 mg), which was purified by preparative TLC (1 plate) over silica gel with ether–benzene (1:1) to yield a crystalline substance (32.5 mg), which was identical with an authentic sample of **25B** in all respects.

Compound **25B** (32 mg) was treated with acetone (5 ml) and 60% aq $HClO_4$ (0.05 ml) at room temperature for 30 min under stirring. The mixture was evaporated below 30 °C, made alkaline with 6 M aq ammonia, and extracted with dichloromethane (4×10 ml). The extracts were worked up as usual to leave oily residue (22 mg), containing **25B** regenerated during work-up, which was submitted to chromatography over alumina (3 g). Less polar fractions eluted with benzene gave an oily material (2.3 mg), showing a single spot on TLC, which was identified as the corresponding acetonide (**27B**), oily; MS, *m/e* 342 (M^+), 327, 284, and 269; IR, ν_{max} ($CHCl_3$) 1665 and 1618 cm^{-1}; NMR, δ 1.07 and 1.26 (each 3H, s, 19- and 18-H), 1.33 and 1.40 (each 3H, s, acetonide CH_3), 4.14 (1H, br, W_H=14 Hz, 17-H), and 5.81 (1H, s, 4-H). Eluates with chloroform afforded the unchanged glycol (**25B**, 17 mg).

To a suspended mixture of chromium(VI) oxide (CrO_3, 27 mg) in dichloromethane (0.3 ml) and pyridine (2 drops) was added **25B** (6.3 mg) in dichloromethane (0.3 ml). The mixture was stirred at room temperature for 30 min and then diluted with ether (10 ml). The ether–dichloromethane solution was washed 5% aq sodium hydroxide, 2M hydrochloric acid (HCl), 5% aq $NaHCO_3$, and saturated brine, dried and evaporated to leave oily residue (6.7 mg), showing 3 spots on TLC. The mixture was separated by preparative TLC (10×20 cm^2, 1 plate) with benzene–ether (1:1). A less polar fraction gave a crystalline substanec (0.4 mg), which was identical with the reaction product (**28B**) of **10A** described later. A more polar fraction yielded formyl ketone (**29B**, 2.0 mg), oily, showing a single spot on TLC, which exhibited the following spectra; MS, *m/e* 300 (M^+), 257, 256, and 213; IR, ν_{max} ($CHCl_3$) 2700, 1723, 1710, 1668, and 1620 cm^{-1}; NMR, δ 1.02 and 2.20 (each 3H, s, 19-H and CH_3CO), 3.65 (1H, br, W_H=12 Hz, 12-H), 5.85 (1H, s, 4-H), and 9.74 (1H, d, J=5 Hz, CHO). A most polar fraction gave the starting glycol (**25B**, 1.3 mg).

*Reaction of 12β,13β-Epoxy-17β-hydroxy-13-epietiojerv-5-en-3-one 17-Acetate 3,3-Ethylene Acetal (**7A**) with BF_3.* Compound **7A** (100 mg) was treated with BF_3 (0.03 ml) in benzene (40 ml) at room temperature for 30 s under stirring, when the spot of **7A** had disappeared on TLC. The reaction mixture was worked up as described above to leave amorphous residue, which was separated roughly into two fractions by chromatography over silica gel (5 g) with benzene–ether mixtures. Fractions eluted with benzene–ether (3:1) were further purified by preparative TLC (3 plates) over silica gel with benzene–ether (2:1) to give 17-acetate (**26A**, 51 mg) of **25A**,

mp 232—234 °C (from ether) and $[\alpha]_D$ +19.2°; MS, 388 (M^+), 373, 370, 355, 328, and 313; UV, λ_{max} 205 nm (ε 6000); IR, ν_{max} 3507, 1719, 1260, 1105, 1088, 1028, and 1019 cm^{-1}; NMR, δ 0.92, 1.13, and 2.09 (each, 3H, s, 19- and 18-H, and OCOCH$_3$), 3.94 (4H, s, OC$_2$H$_4$O), 4.77 (1H, do d, J=10 and 5 Hz, 17-H), and 5.30 (1H, br, W_H=8 Hz, 6-H). Found: C, 70.82; H, 8.21%. Calcd for $C_{23}H_{32}O_5$: C, 71.10; H, 8.30%. Fractions eluted with benzene–ether (2:1 and 1:1) were purified in the same manner as mentioned above to give 17-acetate (**26B**, 20 mg) of **25B**, mp 123—124 °C (from ether) and $[\alpha]_D$ +88.0°; MS, *m/e* 344 (M^+), 326, 284, and 266; UV, λ_{max} 232 nm (ε 12000) and 210 (12000); IR, ν_{max} 3400, 1748, 1673, 1250, 1050, and 1040 cm^{-1}; NMR, δ 1.09, 1.15, and 2.08 (each 3H, s, 19- and 18-H, and OCOCH$_3$), 4.78 (1H, do d, J=10 and 5 Hz, 17-H), and 5.77 (1H, s, 4-H). Found: C, 72.89; H, 8.12%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

*Reaction of 12β,13β-Epoxy-17α-hydroxy-13-epietiojerv-5-en-3-one 3,3-Ethylene Acetal (**8A**) with BF_3.* To a benzene solution (50 ml) of **8A** (150 mg) was added BF_3 (0.05 ml) in benzene (2 ml) under stirring. The solution was stirred at room temperature for 30 s, when the starting alcohol (**8A**) had disappeared on TLC. After addition of ether (25 ml) and 5% aq $NaHCO_3$ (25 ml), the benzene–ether mixture was worked up as usual to leave resinous material, which was submitted to chromatography over silica gel (8 g) with benzene–ether mixtures. Early fractions eluted with benzene–ether (2:1) gave 13β,17α-dihydroxy-12α,13-epietiojerva-5,8(14)-dien-3-one 3,3-ethylene acetal (**31A**, 50 mg), mp 174—175 °C (from ether) and $[\alpha]_D$ −45.8°; MS, *m/e* 346 (M^+), 331, 328, 313, and 284; UV, λ_{max} 207 nm (ε 9000); IR, ν_{max} 3550, 3480, 1100, 1075, 1032, and 1022 cm^{-1}; NMR, δ 0.90 and 1.20 (each 3H, s, 19- and 18-H), 3.70 (1H, br, W_H=8 Hz, 17-H), 3.94 (4H, s, OC$_2$H$_4$O), and 5.34 (1H, br, W_H=8 Hz, 6-H). Found: C, 72.83; H, 8.97%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. Later fractions eluted with benzene–ether (2:1) afforded 13β,17α-dihydroxy-13-epietiojerva-5,12(14)-dien-3-one 3,3-ethylene acetal (**32A**, 30 mg), mp 169—171 °C (from acetone–ether) and $[\alpha]_D$ −3.7°; MS, *m/e* 346 (M^+), 331, 328, 313, 302, and 234; IR, ν_{max} 3400, 1095, and 1058 cm^{-1}; NMR, δ 1.12 and 1.29 (each 3H, s, 19- and 18-H), 3.58 (1H, br, W_H=5 Hz, 17-H), 3.95 (4H, s, OC$_2$H$_4$O), and 5.44 (1H, br, W_H=7 Hz, 6-H). Found: C, 72.68; H, 8.90%. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73%. Fractions eluted with benzene–ether (1:1) gave 13β,17α-dihydroxy-12α,13-epietiojerva-4,8(14)-dien-3-one (**31B**, 42 mg), showing a single spot on TLC, amorphous and $[\alpha]_D$ +59.7°; MS, *m/e* 302 (M^+), 284, and 266; UV, λ_{max} 234 nm (ε 11000) and 208 (9000); IR, ν_{max} 3400, 1650, 1070, and 1018 cm^{-1}; NMR, δ 1.08 and 1.25 (each 3H, s, 19- and 18-H), 3.76 (1H, br, W_H=7 Hz, 17-H), and 5.84 (1H, s, 4-H). Found: C, 75.89; H, 8.34%. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67%.

Compound **31A** (6 mg) was treated with *p*-TsOH (2 mg) in acetone (2 ml) and water (0.5 ml) under reflux for 2 h. The mixture was worked up as usual to give an amorphous substance, showing a single spot on TLC, which was identical with a sample of **31B** (MS, IR, NMR, and TLC).

Compound **32A** (8 mg) was treated with acetic anhydride (0.05 ml) and pyridine (0.1 ml) at room temperature for 24 h under stirring. The mixture was worked up as usual to give 17-acetate (**33A**, 6 mg), mp 119—121 °C (ether) and $[\alpha]_D$ −15.2°; MS, *m/e* 388 (M^+), 373, and 310; IR, ν_{max} 3440, 1735, 1248, and 1100 cm^{-1}; NMR, δ 1.13, 1.20, and 2.05 (each 3H, s, 19- and 18-H, and OCOCH$_3$), 3.96 (4H, s, OC$_2$H$_4$O), 4.77 and 5.44 (each 1H, br, W_H=7 Hz, 17- and 7-H).

To a suspended mixture of CrO_3 (20 mg) in dichloromethane (0.3 ml) and pyridine (2 drops) was added **31B** (6 mg) in dichloromethane (0.4 ml) under stirring. The mixture was stirred vigorously at room temperature for 40 min and diluted with ether. The whole mixture was worked up as described before to leave crystalline residue (5.4 mg), which was purified by preparative TLC (10× 20 cm^2, 1 plate) over silica gel with benzene–ether (1:1). A major fraction gave hydroxy ketone (2.3 mg), mp 176—179 °C, which was identical with a sample of **28B** described before in all respects.

*Reaction of 12β,13β-Epoxy-17α-hydroxy-13-epietiojerv-5-en-3-one 17-Acetate 3,3-Ethylene Acetal (**9A**) with BF_3.* Compound **9A** (140 mg) was treated with BF_3 (0.04 ml) in benzene (50 ml) at room temperature for 1 min under stirring, when the solution became violet. After addition of ether (25 ml) and 5% aq $NaHCO_3$ (25 ml), the mixture was separated into the benzene–ether and aqueous solutions. The former was washed with 5% aq $NaHCO_3$ (50 ml) and water (3× 50 ml), dried and evaporated to leave a complex mixture, which was separated roughly into two fractions by chromatography over silica gel (5 g) with a 1:1 benzene–ether mixture. Early and later eluates (33 and 65 mg) were further purified by preparative TLC (2 and 4 plates) over silica gel, respectively, giving 12α,13β,17α-trihydroxy-13-epietiojerv-5-en-3-one 12-acetate 3,3-ethylene acetal (**35A**, 33 mg) and 12β,13α,17α-trihydroxyetiojerv-5-en-3-one 17-acetate 3,3-ethylene acetal (**34A**, 24 mg). **35A**, amorphous and $[\alpha]_D$ −14.6°; MS, 406 (M^+), 388, 346, and 328; IR, ν_{max} ($CHCl_3$) 3640, 3510, 1708, 1280, 1100, 1010, and 980 cm^{-1}; NMR, δ 1.02, 1.18, and 2.08 (each 3H, s, 19- and 18-H, and OCOCH$_3$), 3.72 (1H, br, W_H=22 Hz, 17-H), 3.95 (4H, s, OC$_2$H$_4$O), and 5.38 (1H, br, W_H=8 Hz, 6-H). Found: C, 67.40; H, 8.77%. Calcd for $C_{23}H_{34}O_6$: C, 67.95; H, 8.43%. **34A**, mp 217—219 °C (from ether) and $[\alpha]_D$ −22.5°; MS, *m/e* 406 (M^+), 388, 346, and 328; IR, ν_{max} 3608, 3550, 1728, 1260, 1110, 1023, and 990 cm^{-1}; NMR, δ 1.03, 1.22, and 2.09 (each 3H, s, 19- and 18-H, and OCOCH$_3$), 3.95 (4H, s, OC$_2$H$_4$O), 5.14 (1H, br, W_H=17 Hz, 17-H), and 5.41 (1H, br, W_H=8 Hz, 6-H). Found: C, 67.92; H, 8.55%. Calcd for $C_{23}H_{34}O_6$: C, 67.95; H, 8.43%.

Compound **34A** (6 mg) was treated with 5% KOH in methanol (1 ml) at room temperature for 5 h under stirring. The reaction mixture was worked up as usual to leave crystalline residue (4.8 mg), which was recrystallized from ether to give the corresponding triol (**36A**), mp 207.5—208.5 °C; MS, *m/e* 364 (M^+), 346, 328, and 99; IR, ν_{max} ($CHCl_3$) 3605, 3470, 1101, 1017, and 987 cm^{-1}; NMR, δ 1.02 and 1.32 (each 3H, s, 19- and 18-H), 3.87 (1H, br m, W_H= 24 Hz, 17-H), 3.94 (4H, s, OC$_2$H$_4$O), and 5.39 (1H, br, W_H=8 Hz, 6-H). The triol (**36A**, 4.8 mg) was then treated with acetone (2 ml) and 60% aq $HClO_4$ (2 drops, 0.035 ml) at room temperature for 20 h under stirring. The reaction mixture was worked up as usual to give the corresponding 13α,17α-acetonide (**37B**, 4.6 mg), amorphous; MS, *m/e* 360 (M^+), 320, 302, 284; IR, ν_{max} ($CHCl_3$) 3690, 3480, 1661, and 1614 cm^{-1}; NMR, δ 1.14 (3H, s, 19-H), 1.24 and 1.29 (6H, and 3H, each s, 18-H and acetonide CH$_3$), 4.22 (1H, br, W_H=20 Hz, 17-H), and 5.77 (1H, s, 4-H).

Compound **35A** (36 mg) was hydrolyzed with 5% KOH in methanol (2 ml) at room temperature for 20.5 h to give the corresponding triol (**38A**, 26 mg), mp 199.5—201.5 °C (from benzene) and $[\alpha]_D$ −51.7°; MS, *m/e* 364 (M^+), 346, 328, and 99; IR, ν_{max} 3460, 3425 (sh), 1084, 1013, and 985 cm^{-1}; ν_{max} ($CHCl_3$) 3615, 3490, 1105, 1088, 1059, 1019, and 997 cm^{-1}; NMR, δ 1.04 and 1.36 (each 3H, s, 19- and 18-H), 2.60, 2.66, and 2.71 (each 1H, s, 3OH), 3.68 (1H,

br, W_H=14 Hz, and 6 Hz on addition of D_2O, 17-H), 3.94 (4H, s, $OC_2\underline{H}_4O$), and 5.36 (1H, br, W_H=9 Hz, 6-H). The triol (**38A**, 13 mg) was also treated with *p*-TsOH (3 mg) in acetone (2 ml) and water (0.5 ml) under reflux for 2 h. The mixture was worked up as described already to leave crystalline residue (12 mg), which on recrystallization from benzene–diisopropyl ether gave 12α,13β,17α-trihydroxy-13-epietiojerv-4-en-3-one (**38B**, 5.0 mg), mp 197—198 °C and $[\alpha]_D$ +76.6°; MS, *m/e* 320 (M^+), 302, 284, 266, and 84; IR, ν_{max} ($CHCl_3$) 3645, 3455, 1667, 1617, 1060, 1016, and 937 cm^{-1}; NMR, δ 1.14 and 1.37 (each 3H, s, 19- and 18-H), 3.03 (1H, br s, OH), 3.68 (1H, br, W_H=21 Hz, and 9 Hz on addition of D_2O, 17-H), and 5.73 (1H, s, 4-H).

To a suspended mixture of CrO_3 (30 mg) in dichloromethane (0.3 ml) and pyridine (3 drops) was added **38B** (10 mg) in pyridine (0.5 ml). The mixture was stirred at room temperature for 40 min. After addition of ether (50 ml) the reaction mixture was worked up as described before to leave oily residue (6 mg), which was submitted to prepararive TLC (20×10 cm^2, 1 plate) over silica gel to give the starting alcohol (**38B**, 1.3 mg) and 12α,13β-dihydroxy-13-epietiojerv-4-ene-3,17-dione (**39B**, 1.7 mg), mp 171.5—173 °C (from benzene–diisopropyl ether); MS, *m/e* 318 (M^+) and 300; IR, ν_{max} ($CHCl_3$) 3605, 3510, 1715, 1669, and 1619 cm^{-1}; NMR, δ 1.08 and 1.47 (each 3H, s, 19- and 18-H), 1.58 and 3.66 (each 1H, s, 2OH), and 5.79 (1H, s, 4-H). Compound **21B** (9.2 mg) was likewise oxidized with CrO_3 (25 mg) in dichloromethane (0.6 ml) and pyridine (0.2 ml) at room temperature for 45 min under stirring. The reaction mixture was worked up as usual and purified by preparative TLC (1 plate) over silica gel with ether to give the starting alcohol (**21B**, 0.5 mg) and hydroxy ketone, mp 168.5—170 °C, which was identical with a sample of **39B** (MS, IR, NMR, and TLC).

*Reaction of 12β,13β-Epoxy-13-epietiojerv-5-ene-3,17-dione 3,3-Ethylene Acetal (**10A**) with BF_3.* Compound **10A** (50 mg) was treated with BF_3 (0.02 ml) in benzene (20 ml) at room temperature for 20 min under stirring, when the spot of **10A** had disappeared on TLC. The reaction was ceased by addition of ether (10 ml) and 5% aq $NaHCO_3$ (10 ml), and the mixture was worked up as mentioned above to leave amorphous residue, showing essentially a single spot on TLC, which was purified by preparative TLC (3 plates) over silica gel with a 6:4:1 mixture of benzene, ether, and chloroform to give 13β-hydroxy-12α,13-epietiojerva-4,8(14)-diene-3,17-dione (**28B**, 35 mg), mp 178—180 °C and $[\alpha]_D$ +178.2°; MS, *m/e* 300 (M^+), 282 and 214; UV, λ_{max} 232 nm (ε 10000) and 206 (8000); IR, ν_{max} 3370, 1717, 1650, 1610, 1112, and 1083 cm^{-1}; NMR, δ 1.14 and 1.27 (each 3H, s, 19- and 18-H), and 5.83 (1H, s, 4-H). Found: C, 75.69; H, 7.85%. Calcd for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05%. The compound (**28B**) was identified as the aforementioned oxidation product of **25B** by direct comparison of both the samples.

*Reduction of **5A** with Sodium Borodeuteride ($NaBD_4$).* Compound **5A** (1.12 g) was treated with $NaBD_4$ (Merck, D-content 98%, 160 mg) in methanol (100 ml) at room temperature for 30 min under stirring. After addition of acetic acid to decompose excess of the $NaBD_4$, the mixture was made alkaline with 6 M aq ammonia, evaporated below 30 °C, mixed with water and extracted with chloroform. The chloroform extracts were worked up as usual to leave foamy residue (1.27 g), showing two spots on TLC, which was submitted to chromatography over silica gel (80 g) with benzene–ether mixtures. Less polar fractions (220 mg) eluted with benzene–ether (2:1) afforded 12α,13α-epoxy-17β-hydroxyetiojerv-5-en-3-one-17-*d* 3,3-ethylene acetal (**41A**, 161 mg), mp 154.5—157 °C (from benzene–diisopropyl ether) and $[\alpha]_D$ −75.2°; MS, *m/e* 348 (0.25%), 347 (M^+, 0.66%), 329 (0.27%), and 99 (base); IR, ν_{max} 3470, 1115, 1100, 1028, 997, and 963 cm^{-1}; NMR, δ 1.00 and 1.37 (each 3H, s, 19- and 18-H), 1.60 (1H, s, OH), 3.95 (4H, s, $OC_2\underline{H}_4O$), and 5.38 (1H, br, W_H=11 Hz, 6-H). More polar fractions eluted with benzene–ether (2:1 and 1:1) gave a 17β-epimer (α-OH) (**40A**, 890 mg), mp 169—171 °C (from benzene–diisopropyl ether) and $[\alpha]_D$ −57.8°; MS, *m/e* 348 (0.24%), 347 (M^+, 0.59%), 329 (0.33%), and 99 (base); IR, ν_{max} 3480, 1136, 1090, 1070, 1047, 961, and 946 cm^{-1}; NMR, δ 1.00 and 1.39 (each 3H, s, 19- and 18-H), 1.68 (1H, s, OH), 3.95 (4H, s, $OC_2\underline{H}_4O$), and 5.38 (1H, br, W_H=10 Hz, 6-H). The R_f values of **40A** and **41A** on TLC were identical with those of **1A** and **3A**, respectively.

Compound **40A** (20 mg) was oxidized with CrO_3 (242 mg) in pyridine (5.1 ml) at room temperature for 17 h under stirring. The reaction mixture was worked up as mentioned above to leave oily residue (21 mg), showing two spots on TLC, which was separated by chromatography over silica gel (1.5 g) with benzene–ether (2:1). Less polar fractions gave a crystalline substance (6.7 mg) on trituration with diisopropyl ether, which had mp 143.5—144 °C and was identified as **5A** by direct comparison of both the samples. More polar fractions afforded the unchanged alcohol (**40A**, 12.3 mg). Compound **41A** (15 mg) was likewise oxidized with CrO_3 (173 mg) in pyridine (4.5 ml) at room temperature for 17 h to give **5A** (8.2 mg), mp 143.5—144 °C, and the unchanged alcohol (**41A**, 6 mg).

*Reaction of **40A** with BF_3.* To a benzene solution (100 ml) of **40A** (452 mg) cooled with ice-water was added rapidly BF_3 (0.2 ml), freshly distilled over calcium hydride, in benzene (3 ml) under stirring. The mixture was stirred at room temperature for 30 s. The reaction was ceased by addition of 5% aq $NaHCO_3$ (50 ml). The whole mixture was separated into the benzene and aqueous layers, and the latter was shaken with ether (2×50 ml). The benzene and ether solutions were combined, washed with 5% aq $NaHCO_3$ (3×30 ml) and saturated brine (3×30 ml), dried and evaporated below 30 °C to leave foamy residue (437 mg), showing two major spots on TLC, which was separated by chromatography over silica gel (30 g) with benzene–ether (19:1). Less polar fractions afforded a crystalline substance (51 mg) on trituration with diisopropyl ether–hexane, which on recrystallization from ether gave a 17-*d* derivative (**43A**, 13 mg) of **17A**, mp 116—118.5 °C and $[\alpha]_D$ −81.0°; MS, *m/e* 312 (0.87%), 311 (M^+, 2.48%), 310 (0.20%), and 99 (base); IR, ν_{max} ($CHCl_3$) 1104 and 1094 cm^{-1}; NMR, δ 1.16 and 2.27 (each 3H, s, 19- and 18-H), 3.95 (4H, s, $OC_2\underline{H}_4O$), 5.49 (1H, br, W_H=10 Hz, 6-H), 6.97 and 7.06 (each 1H, ABq, J=8 Hz, 15- and 16-H). More polar fractions afforded a crystalline substance (79 mg) on trituration with diisopropyl ether, which was recrystallized from ether to give a 13-*d* derivative (**42A**, 24 mg) of **11A**, mp 133—135 °C and $[\alpha]_D$ −63.2°; MS, *m/e* 330 (0.67%), 329 (M^+, 1.73%), 328 (0.50%), and 99 (base); IR, ν_{max} 1722, 1109, and 1096 cm^{-1}; NMR, δ 1.09 and 1.21 (each 3H, s, 19- and 18-H), 3.96 (4H, s, $OC_2\underline{H}_4O$), and 5.43 (1H, br, W_H=10 Hz, 6-H).

Compound **42A** (25 mg) was treated with 5% KOH in methanol (1 ml) at room temperature for 1 h. The reaction mixture was evaporated, diluted with water, acidified to pH 6 with 2 M aq HCl, and extracted with chloroform (4×10 ml). The chloroform extracts were worked up as usual to leave amorphous residue (23 mg), which was purified by preparative TLC over silica gel (1 plate) with benzene–ether (3:1). Major fractions gave a crystalline substance

(13 mg) on trituration with diisopropyl ether, which had mp 164.5—166 °C and was identical with a sample of **12A** (MS, IR, NMR, and TLC).

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