12,13-Epoxy-*C*-nor-*D*-homosteroids. VII.[1] Reaction of 11-Oxygenated 17α-Acetyl-12β,13β-epoxy-13-epietiojervanes with Boron Trifluoride Etherate and Potassium Hydroxide[2]

Akio Murai, Hiroshi Sasamori, and Tadashi Masamune*

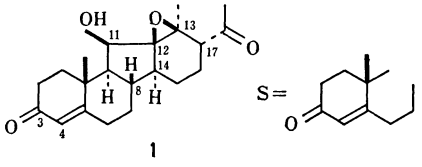
Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060

(Received July 11, 1979)

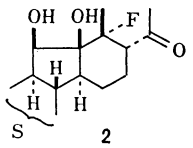
The title compounds were treated with boron trifluoride etherate in benzene at room temperature. 11β-Hydroxy- and 11-oxo-12β,13β-epoxides (**1** and **14**) underwent cleavage of the epoxy group at C-13 by the acid treatment to give the corresponding fluorohydrins (**2** and **5**) as the respective major products, while the former (**1**) also afforded a 13β-pregnane derivative (**3**) with a normal steroid skeleton. On the other hand, several 11-oxygenated 12α,13α- and 12β,13β-epoxides (**17**, **17a**, **19**, **21**, **1**, and **23**) were treated with potassium hydroxide in aqueous methanol at room temperature. All epoxides gave the corresponding $\Delta^{13(17)}$-20-ketones, and only 11-hydroxy- and 11-acetoxy-12α,13α-epoxides (**17**, **19**, and **17a**) were further transformed into a 13α-pregnane derivative (**12**).

In a previous paper[3] we reported the synthesis and stereochemistry of 17α-acetyl-12,13-epoxyetiojervanes. As a continuing study aimed at the preparation of normal steroids from jervine, we have examined reactions of 11-oxygenated 17α-acetyl-12β,13β-epoxy-13-epietiojervanes[3] with boron trifluoride etherate and potassium hydroxide, considering the reaction of the corresponding 12α,13α-epoxyetiojervanes.[4] In the present paper we describe the result, which involves transformation into a compound with a pregnane skeleton.

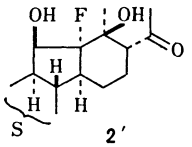
Acid Treatment. Treatment of 17α-acetyl-12β,13β-epoxy-11β-hydroxy-13-etiojerv-4-en-3-one[3] (**1**) with boron trifluoride etherate (BF_3) in benzene at room temperature for 30 s produced a mixture, from which three compounds (**2**—**4**) were isolated after careful chromatography in 38, 16 and 10% yields, respectively. The major product (**2**), mp 228—230 °C, was assigned on the basis of the following evidence. The mass [*m/e* 364 (M^+), 344 (M^+—HF), and 301 (344—$COCH_3$)] and NMR spectra [δ 2.22 (3H, s, 21-H), 3.29 (1H, d, J=6 Hz, 11-OH), 3.72 (1H, s, OH)] revealed the presence of one fluorine atom, one acetyl (at C-17) and two hydroxyl groups. These spectra, coupled with the UV [λ_{max} 239 nm (ε 11000)] and IR spectra (ν_{max} 1702 cm^{-1}), indicated that the A ring and 17-side chain remained unchanged. The NMR spectrum also exhibited two three-proton singlets at δ 1.40 and 1.42 (19- and 18-H or *vice versa*) and one-proton doublet (J=8 Hz) due to a proton on the carbon atom (at C-11) bearing the hydroxyl group at δ 4.57. Compound **2**, when oxidized with the Jones reagent, was converted into hydroxy ketone (**5**), mp 198—200 °C, in 75% yield, which showed a strong absorption maximum at 1748 cm^{-1} in the IR spectrum, indicating the secondary hydroxyl group is located on a five-membered (C) ring. Compound **2** also formed the acetonide (**6**), oil, by prolonged treatment (42 h) with acetone and aeid ($HClO_4$) in 47% yield, with the recovered fluorohydrin (**2**, 50%), indicative of the presence of a *cis*-glycol moiety. Moreover, the fluorohydrin (**2**) underwent dehydrofluorination by treatment with base (KOH in aq CH_3OH, room temp, 3.5 h) to give $\Delta^{13(17)}$-20-ketone (**7**), mp 154—156 °C, showing an absorption maximum at 245 nm (ε 17000) and two three-proton singlets at δ 1.39 and 1.86 (19- and 18-H) in the UV and NMR spectra. This compound (**7**), when treated with BF_3 at room temperature for 30 s, was transformed into a known Δ^{12}-11,17-dione[3] (**8**) in 40% yield. All these facts indicate that the major compound should be assigned formula **2**, excluding an alternate structure (**2'**). The configuration of the fluorine atom at C-13 was assigned by analogy of *trans*-fluorohydrin formation[4] resulting from the epoxide cleavage by the S_N2 type of nucleophilic attack of a fluoride anion.[5]



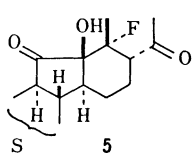
1



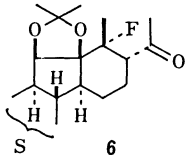
2



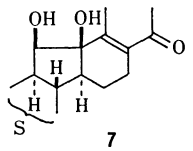
2'



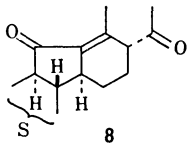
5



6



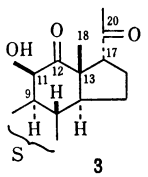
7



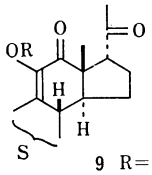
8

The second product (**3**), oil, had the same molecular formula $C_{21}H_{28}O_4$ as the starting epoxide (**1**), and its spectra revealed the presence of hydroxyl, acetyl, and Δ^4-3-carbonyl groups: OH, *m/e* 344 (M^+) and 326 (M^+-H_2O); ν_{max} 3483 cm^{-1}; δ 3.80 (1H, d, J=4 Hz, OH): CH_3C=O, ν_{max} 1713 cm^{-1}; δ 2.18 (3H, s, 21-H): Δ^4-3-C=O, λ_{max} 239 nm (ε 13000); ν_{max} 1664

and 1616 cm^{-1}; δ 5.72 (1H, s, 4-H). Hence the remaining oxygen atom would consititute a carbonyl group on a six-membered ring, whose absorption maximum might overlap with that of the acetyl carbonyl group (1713 cm^{-1}),[6] or an ether oxygen function. The possibility of the latter was excluded by the following facts. Compound **3**, when oxidized with the Jones reagent, was converted into diosphenol (**9**), mp 142—144 °C, in 75% yield. The diosphenol structure was characterized by the spectra of **9** and its acetate (**9a**): **9**, λ_{max} 284 nm (ε 7000);[7] ν_{max} 3400, 1664, and 1620 cm^{-1}; δ 6.91 (1H, s, OH) and no signal due to a proton at C-11: **9a**, λ_{max} 243 nm (ε 20000) ($\Delta^{9(11)}$-12-C=O and Δ^{4}-3-C=O); ν_{max} 1766, 1621, and 1225 cm^{-1}; δ 2.28 (3H, s, $OCOCH_3$), 1.12 and 1.53 (each 3H, s, 18- and 19-H), and 3.55 (1H, do d, J=12.5 and 6 Hz, 17-H). The formation of diosphenol **9** suggested strongly that an α-ketol group is located in a six-membered ring in **3** and hence the compound (**3**) must possess a normal steroid skeleton. In order to confirm the structure, compound **3** was treated with base (KOH in aq CH_3OH, room temp, 16 h) with expectation that **3** would be transformed into a known steroidal compound[8] (**10**). However, the treatment led to formation of hemiacetal (**11**). oil, in 40% yield, whose structure was deduced from the spectral data; ν_{max} 3600, 3430, 1718, 1667, and 1614 cm^{-1}; δ 1.13, 1.32 and 1.41 (each 3H, s, 18-, 19- and 21-H, or *vice versa*), 4.22 and 5.72 (each 1H, s, 12- and 4-H). The spectra were similar to but not identical with those of the corresponding 13α-pregnane[4] (**12**). The compound (**3**) is therefore represented by the 13β-pregnane formula (**3**) most favorably. The formation of hemiacetal **11** rather than **10** would probably result from facile epimerization of the α-ketol system under the basic conditions, compared with that of the 17-acetyl group.

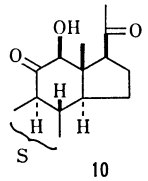


3

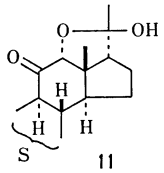


9 R=H

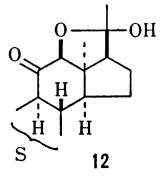
9a R=Ac



10

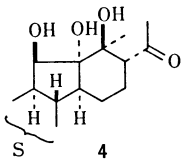


11

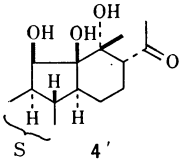


12

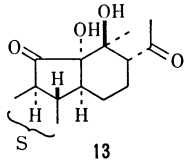
The third product (**4**), mp 188—190 °C, was tentatively assigned formula **4**. The molecular formula $C_{21}H_{30}O_5$ [(**1**) $C_{21}H_{28}O_3+H_2O$], coupled with the spectral data, suggested that the compound would be formed by hydrolysis of the epoxy group and formulated by **4** or **4'**: OH, *m/e* 362 (M^+), 344 (M^+-H_2O) and 326 (M^+-2H_2O); ν_{max} 3360 cm^{-1}; δ 4.46 (1H, d, J=6 Hz, 11-H) and 1.34 (3H, s, 18-H): 17-$COCH_3$, ν_{max} 1693 cm^{-1}; δ 3.15 (1H, br, W_H=18 Hz, 17-H) and 2.26 (3H, s, 21-H): Δ^4-3-C=O, λ_{max} 239 nm (ε 13000); ν_{max} 1661 and 1613 cm^{-1}; δ 1.38 (3H, s, 19-H) and 5.70 (1H, s, 4-H). Oxidation of **4** with chromium(VI) oxide gave a five-membered hydroxy ketone (**13**), mp 198—200 °C, showing an absorption maximum at 1747 cm^{-1} in the IR spectrum. The compoumd (**4**) was then treated with periodic acid (aq dioxane, room temp, 18 h), when none of the acid had been consumed. Moreover, it did not give the acetonide under the same conditions as **2**. These results are in good accord with formula **4** with two *trans*-glycol systems for the third compound. The formation of **4** would probably take place in acidic media during the work-up.



4

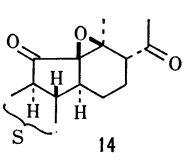


4'

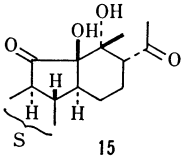


13

Similar and slightly prolonged (10 min) treatment of 17α-acetyl-12β,13β-epoxy-13-epietiojerv-4-ene-3,11-dione[3] (**14**) with BF_3 producted two compounds in 63 and 18% yields. The major product, mp 198—200 °C, was identified as fluorohydrin **5** described already. The minor product (**15**), mp 221—223 °C, had a molecular formula $C_{21}H_{38}O_4$ [(**14**) $C_{21}H_{26}O_3+H_2O$] and displayed the mass, UV, and IR spectra (except the finger print region) similar closely to those of compound **13**. However, the NMR spectrum revealed the presence of two hydroxyl groups at δ 4.20 and 7.24 (each 1H, s) and differed clearly from that of **13**. These data led to tentative assignment of formula **15** to the compound. It is beyond our comprehension that 12β,13β-epoxyetiojervanes (**1** and **14**) gave compounds formulated by simple hydrolysis products (**13** and **15**) though in low yield, while such compounds were not isolated from 12α,13α-epoxyetiojervanes.[4] In summary, the reactions of 12β,13β-epoxyetiojervanes with the acid resembled those of the corresponding 12α,13α-epimers as far as the predominant formation of fluoro-



14



15

hydrins concerns, but differed definitely in the one-step transformation into the 13β-pregnane derivative (**3**).

Base Treatment. We previously reported that base treatment of 17α-acetyl-13β-fluoro-11α,12α-dihydroxy-13-epietiojerv-4-en-3-one (**16**), a major product obtained by the BF_3 treatment of the corresponding 12α,13α-epoxide (**17**), gave rise to a 13α-pregnane derivative (**12**) *via* 11α,12α-dihydroxy-$\Delta^{13(17)}$-20-ketone (**18**).[4] In connection with the interesting rearrangement, we examined reactions of several 11-oxygenated 17α-acetyl-12,13-epoxyetiojervanes with base. The results (Table 1) are summarized as follows.

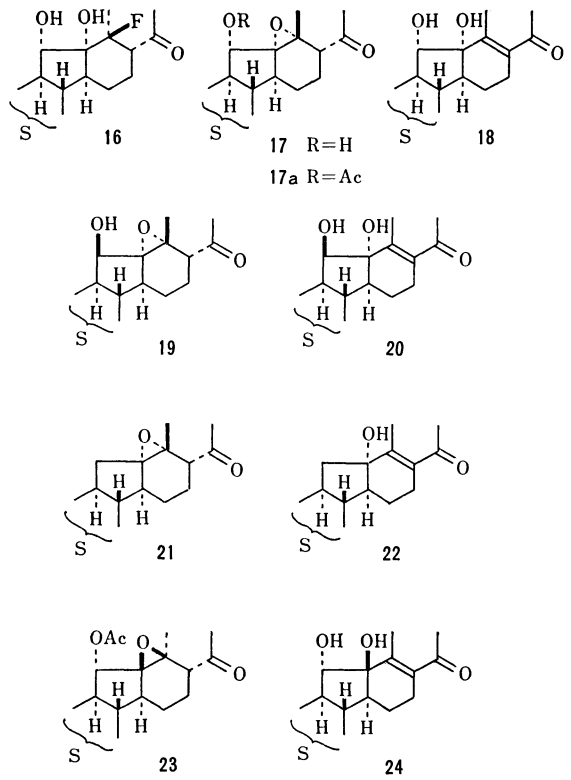
Table 1. The reaction of 11-oxygenated 17α-acetyl-12,13-epoxyetiojervanes with base[a]

Starting 12,13-epoxide	Reaction time/h	Products (isolated yield/%) $\Delta^{13(17)}$-20-ketone		13-pregnane	
11α-OH, α-epoxide (**17**)	2.5	(**18**)	15	(**12**)	65
	19	(**18**)	0	(**12**)	75
11α-OAc, α-epoxide (**17a**)	1.6	(**18**)	56	(**12**)	40
	19	(**18**)	10	(**12**)	67
11β-OH, α-epoxide (**19**)	1.6	(**20**)	70	(**12**)	20
	2.5	(**20**)	55	(**12**)	25
	19	(**20**)	0	(**12**)	75
11-deoxo, α-epoxide (**21**)	1.6	(**22**)	100		0
	19	(**22**)	70		0
11β-OH, β-epoxide (**1**)	1.6	(**7**)	90		0
	19	(**7**)	75		0
11α-OAc, β-epoxide (**23**)	19	(**24**)	70		0

a) KOH in aq CH_3OH, room temp.

(i) The base treatment of 11α-hydroxy-12α,13α-epoxide[3] (**17**) and its 11-acetate[3] (**17a**) afforded **18** and **12**. Likewise, 11β-hydroxy-12α,13α-epoxide[3] (**19**) was converted into the corresponding 11β,12α-dihydroxy-$\Delta^{13(17)}$-20-ketone (**20**) and **12**. However, (ii) the reaction of 11-unsubstituted 12α,13α-epoxide[3] (**21**) resulted in formation of only the corresponding $\Delta^{13(17)}$-20-ketone (**22**). Moreover, 11β-hydroxy-12β,13β-epoxide (**1**) and its 11α-acetoxy isomer[3] (**23**) produced only 11β,12β- and 11α,12β-dihydroxy-$\Delta^{13(17)}$-20-ketones (**7** and **24**) under almost the same conditions, no 13β-pregnane derivatives (**3** and **11**) being isolated. The structure of these new compounds (**20**, **22**, and **24**) were deduced from their spectral data. Compounds **20**, mp 221—223 °C, **22**, mp 169.5—171.5 °C, and **24**, mp 212—214 °C, exhibited the same absorption maximum at 245 nm (ε 17000) as the known $\Delta^{13(17)}$-20-ketones (**7** and **18**) and also three three-proton singlets at δ 1.36, 1.91, and 2.29 (19-, 18- and 21-H), δ 1.07, 1.90, and 2.25, and δ 1.21, 1.97, and 2.25, respectively. The configuration of 11-hydroxyl groups in **20** and **24** were drawn from the chemical shifts of the respective 19-methyl protons (δ_{calcd} 1.36 for **20** and 1.17 for **24**), the contribution of 12-hydroxyl groups being neglected.[9]

Detailed examination of Table 1 reveals the following points. (i) All the epoxides (**17**, **17a**, **19**, **21**, **1**, and **23**) readily gave the respective $\Delta^{13(17)}$-20-ketones (**18**, **18**, **20**, **22**, **7**, and **24**) by base treatment, and the former



two (**18** and **20**) were intermediates for the formation of the 13α-pregnane (**12**). (ii) The reaction of 11α-acetoxy-12α,13α-epoxide (**17a**) proceeded slowly than that of 11α-hydroxy-12α,13α-epoxide (**17**), because the former involved hydrolysis of the 11α-hydroxyl group as the first step. (iii) It should be noted that (a) the formation of 13α-pregnane **12** required the presence of not only a 12α-hydroxyl group but also a hydroxyl group at C-11, whatever the configuration was, and (b) the rearrangement of *cis* (11α,12α)-glycol (**18**) took place more rapidly than *trans* (11β,12α)-glycol (**20**), indicative of serious participation of the 11-hydroxyl group in the rearrangement. The fact that only the compounds possessing 11- and 12α-hydroxyl groups were transformed into the rearranged product (**12**) would be interpreted by assuming that the cleavage of the C-12–C-14 bond and formation of the C-13–C-14 bond would occur from the β-side of the molecule in a concerted manner. We again emphasize that the 13β-pregnane (**3**) was produced from the 11β-hydroxy-12β,13β-epoxide (**1**) only by acid treatment but not by base treatment, while the 13α-pregnane (**12**) from the 11-hydroxy-12α,13α-epoxides (**17** and **19**) only by base treatment.

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) sulfate in dil sulfuric acid and/or iodine. The optical rotations, UV, and IR spectra were measured in chloroform, ethanol, and chloroform, respectively, unless otherwise stated. The NMR spectra were obtained in chloroform-*d* at 100 MHz, and the chemical shifts were given in δ-values, TMS being used as an internal reference. The abbreviations "s, d, t, br, and

do" in the NMR and IR spectra denote "singlet, doublet, broad, and double," respectively.

Treatment of 17α-Acetyl-12β,13β-epoxy-11β-hydroxy-13-epietiojerv-4-en-3-one (1) with Boron Trifluoride Etherate (BF_3). A solution of **1** (90 mg) in anhydrous benzene (9 ml) was stirred with BF_3 (0.18 ml), freshly distilled over calcium hydride, at room temperature for 30 s. The solution was mixed with ether (5 ml), washed with 5% aq sodium hydrogencarbonate and water, dried over anhydrous sodium sulfate, and evaporated to leave amorphous residue (100 mg), which was separated into three fractions by preparative TLC over silica gel (Wakogel B-5F, 10 plates) with ether. A most mobile fraction gave a crystalline substance, which was recrystallized from ether to yield 17α-acetyl-13α-fluoro-11β,12β-dihydroxyetiojerv-4-en-3-one (**2**, 35 mg), mp 228—230 °C and $[\alpha]_D$ +156°; MS, UV, IR, and NMR, in the text. Found: C, 69.35; H, 8.20%. Calcd for $C_{21}H_{29}O_4F$: C, 69.20; H, 8.02%. A middle fraction afforded 11β-hydroxy-17-epipregn-4-ene-3,12,20-trione (**3**, 14 mg), oil, $[\alpha]_D$ +45°; MS, UV, IR, and NMR, in the text; NMR, δ 1.51 and 1.21 (each 3H, s, 19- and 18-H), 3.80 and 4.08 (each 1H, d, J= 4 Hz, OH and 11-H). Found: C, 73.03; H, 8.40%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%. A least mobile fraction gave 17α-acetyl-11β,12α,13β-trihydroxy-13-epietiojerv-4-en-3-one (**4**, 10 mg), mp 188—190 °C (from diisopropyl ether–acetone) and $[\alpha]_D$ +129°; MS, UV, IR, and NMR, in the text.

17α-Acetyl-13α-fluoro-12β-hydroxy-etiojerv-4-ene-3,11-dione (5). A solution of **2** (20 mg) in dry acetone (4 ml) was stirred with the Jones reagent (0.24 ml) for 1 h under cooling with ice. After addition of ethanol, the solution was evaporated and shaken with water and chloroform. The chloroform solution was worked up as usual to leave a crystalline substance, showing a single spot, which was recrystallized from acetone–hexane to give **5** (15 mg), mp 198—200 °C and $[\alpha]_D$ −5.5°; ORD, $[\phi]_{344}^{trough}$ −3900°, $[\phi]_{300}^{peak}$ +4250°, a= −82°; MS, *m/e* 362 (M^+), 344 (M^+-H_2O), 342 (M^+−HF), and 299 (342−$COCH_3$); UV, λ_{max} 235 nm (ε 10000); IR, ν_{max} 3400, 1748, 1707, 1664, and 1614 cm^{-1}; NMR, δ 1.21, 1.50 and 2.20 (each 3H, s, 19-, 18- and 21-H), and 5.80 (1H, s, 4-H).

11,12-Acetonide (6) of 2. A solution of **2** (40 mg) in acetone (8 ml) was stirred with 60% aq perchloric acid (0.4 ml) for 42 h. The solution was made alkaline with 5% aq sodium hydrogencarbonate, evaporated and extracted with chloroform. The chloroform solution, after being worked up as usual, left an oily residue (50 mg), showing two spots, which was separated into two fractions by preparative TLC over silica gel (Wakogel B-5F, 2 plates) with ether. A less polar fraction gave **6** (20 mg), oil; IR, ν_{max} 1705, 1664, 1615, 1384, and 1373 cm^{-1}; NMR, δ 1.39 and 2.17 (6H and 3H, each s, 19-, 18- and 21-H), 1.47 and 1.55 (each 3H, s, acetonide 2CH_3), 3.00 (1H, br, W_H=20 Hz, 17-H), 4.74 (1H, d, J=4 Hz, 11-H), and 5.71 (1H, s, 4-H). Found: C, 71.33; H, 8.07%. Calcd for $C_{24}H_{33}O_4F$: C, 71.26; H, 8.22%. A more polar fraction (20 mg) was identified as the starting fluorohydrin (**2**).

17-Acetyl-11β,12β-dihydroxyetiojerva-4,13(17)-dien-3-one (7). a) A solution of **2** (10 mg) in methanol (2.5 ml) containing 5% potassium hydroxide was stirred at room temperature for 3.5 h. The solution was made neutral with 10% aq acetic acid, evaporated below 40 °C, and shaken with water and chloroform. The chloroform solution gave a crystalline substance, showing a single spot, which was recrystallized from diisopropyl ether–acetone to yield **7**, (8 mg), mp 154—156 °C; MS, *m/e* 344 (M^+), 326, and 311; UV, λ_{max} 245 nm (ε 17000); IR, ν_{max} 3624, 3450, 1680 (br), 1658, and 1612 cm^{-1}; NMR, δ 1.39, 1.86, and 2.25 (each 3H, s, 19-, 18-, and 21-H), 3.36 (1H, d, J=9 Hz, OH), 4.33 (1H, t, J= 9 Hz, 11-H), and 5.67 (1H, s, 4-H).

b) A solution of **7** (20 mg) in anhydrous benzene (2 ml) was stirred with freshly distilled BF_3 (0.04 ml) at room temperature for 30 s. The solution was worked up as usual to leave an oily residue (19 mg), which was separated by preparative TLC over silica gel (Wakogel B-5F, one plate) with ether. A major fraction was crystallized on trituration with diisopropyl ether–acetone and recrystallized from the same solvent mixture to give Δ^{12}-11,20-dione (**8**, 7 mg), which was identified as the known compound.[3]

11-Hydroxy-17-epipregna-3,11-diene-3,12,20-trione (9) and Its 11-Acetate (9a). a) A solution of **3** (8 mg) in dry acetone (1.5 ml) was stirred with the Jones reagent (0.05 ml) for 1 h under cooling with ice. The reaction mixture was worked up as described before to leave an oily substance, which was purified by preparative TLC to yield diosphenol (**9**, 6 mg), mp 142—144 °C; UV, λ_{max} 237 nm (ε 12000) and 284 (7000); IR, ν_{max}3400, 1712, 1664, 1620, and 1613 cm^{-1}; NMR, δ 1.11, 1.53, and 2.14 (each 3H, s, 18-, 19-, and 21-H), 5.77 (1H, s, 4-H), and 6.91 (1H, s, OH). Found: C, 73.41; H, 7.86%. Calcd for $C_{21}H_{26}O_4$: C, 73.66; H, 7.66%.

b) Compound **9** (6 mg) was stirred with acetic anhydride (0.2 ml) and pyridine (0.4 ml) at room temperature for 12 h. The reaction mixture was worked up as usual to give enol acetate (**9a**, 6.4 mg), oil; UV, IR, and NMR, in the text.

12α-Hydroxy-17-epipregn-4-ene-3,11,20-trione 12,20-Hemiacetal (11). A solution of **3** (10 mg) in methanol (2.5 ml) containing 5% potassium hydroxide was stirred at room temperature for 16 h. The reaction mixture was made neutral, evaporated, and shaken with water and chloroform. The chloroform solution was worked up as usual to leave an oily substance, which was purified by preparative TLC to give hemiacetal (**11**, 4 mg), oil and $[\alpha]_D$ +96°; MS, *m/e* 344 (M^+), 326, 311, 301, 284, 283, and 256; UV, λ_{max} 237 nm (ε 10000); IR and NMR, in the text.

17α-Acetyl-12α,13β-dihydroxy-13-epietiojerv-4-ene-3,11-dione (13). To a stirred suspension of chromium(VI) oxide (15 mg) in dry dichloromethane (0.4 ml) and pyridine (0.025 ml) was added a solution of **4** (8 mg) in dichloromethane (0.1 ml). The mixture was stirred at room temperature for 15 min and filtered, then precipitates were washed with ether. The filtrate and ether washings were combined, washed with 5% aq sodium hydroxide and saturated aq sodium chloride, dried and evaporated to leave a crystalline substance (7 mg), which was recrystallized from ether to yield **13** (4 mg), mp 198—200 °C; MS, *m/e* 360 (M^+), 342, 318, 300, and 285; UV, λ_{max} 238 nm (ε 12000); IR, ν_{max} 3440, 1747, 1710, 1665, and 1612 cm^{-1}; NMR, δ 1.23, 1.46, and 2.20 (each 3H, s, 19-, 18- and 21-H), 4.20 (1H, s, OH), 5.76 (1H, s, 4-H), and 7.24 (1H, s, OH).

Treatment of 17α-Acetyl-12β,13β-epoxy-13-epietiojerv-4-ene-3,11-dione (14) with BF_3. Compound **4** (30 mg) in benzene (3 ml) was treated with BF_3 (0.07 ml) at room temperature for 10 min. The reaction mixture was worked up as described before to give oily residue (34 mg), which was separated into two fractions by preparative TLC over silica gel (Wakogel B-5F, 2 plates) with ether. A less polar fraction gave 11-oxo fluorohydrin (20 mg), mp 198—200 °C (from acetone–hexane), which was identified as **5**. A more polar fraction afforded 17α-acetyl-12β,13α-dihydroxyetiojerv-4-ene-3,11-dione (**15**, 6 mg), mp 221—223 °C and $[\alpha]_D$ −2.2°; MS, *m/e* 360 (M^+), 342, 318, 300, and 285; UV, λ_{max} 238 nm (ε 12000); IR, ν_{max} 3443, 1743, 1713, 1664, and 1614 cm^{-1};

NMR, δ 1.18, 1.46, and 2.20 (each 3H, s, 19-, 18- and 21-H), 4.20 (1H, s, OH), 5.76 (1H, s, 4-H), and 7.24 (1H, s, OH).

*Base Treatment of 11-Oxygenated 17α-Acetyl-12,13-epoxyetiojervanes (**17**, **17a**, **19**, **21**, **1**, and **23**).* The results are summarized in Table 1, and a few representative examples are described below. a) A solution of 11α-hydroxy-12α,13α-epoxide[3] (**17**, 20 mg) in methanol (5 ml) containing 5% potassium hydroxide was stirred at room temperature for 2.5 h. The reaction mixture was made neutral with 10% aq acetic acid under cooling, evaporated below 40 °C, and shaken with water and chloroform. The chloroform solution was worked up as usual to leave oily residue, showing two spots on TLC, which was separated into two fractions by preparative TLC over silica gel (Wakogel B-5F, one plate). A less polar fraction (13 mg) was identified as a known 13α-pregnane derivative[4] (**12**) by direct comparison with the sample (MS, NMR, IR, and TLC). A more polar fraction (3 mg) was also identified as 11α,12α-dihydroxy-$\Delta^{13(17)}$-20-ketone[4] (**18**).

b) Treatment of 11β-hydroxy-12α,13α-epoxide[3] (**19**, 20 mg) with potassium hydroxide under the same conditions (2.5 h) as mentioned above afforded **12** (5 mg) and 11β,12α-dihydroxy-$\Delta^{13(17)}$-20-ketone (**20**, 11 mg) after preparative TLC, mp 221—223 °C; MS, *m/e* 344 (M^+); UV, λ_{max} 245 nm (ε 16000); IR, ν_{max} 3540, 3380, 1690 (br), 1655, and 1608 cm^{-1}; NMR, δ 1.36, 1.91, and 2.29 (each 3H, s, 19-, 18-, and 21-H), 4.10 (1H, d, J=4 Hz, 11-H), and 5.71 (1H, s, 4-H).

c) Treatment of 11-unsubstituted 12α,13α-epoxide[3] (**21**, 20 mg) and 11α-acetoxy-12β,13β-epoxide[3] (**23**, 20 mg) were treated with potassium hydroxide under the same conditions (19 h) as described above. The respective reaction mixture was worked up as usual to give 12α-hydroxy- (**22**, 13 mg) and 11α,12β-dihydroxy-$\Delta^{13(17)}$-20-ketones (**24**, 13 mg), 13α- and 13β-pregnane derivatives being not detected on TLC: **22**, mp 169.5—171.5 °C; MS, *m/e* 328 (M^+); UV, λ_{max} 245 nm (ε 17000); IR, ν_{max} 3610, 3444, 1680 (br), 1660, and 1614 cm^{-1}; NMR, δ 1.07, 1.90, and 2.25 (each 3H, s, 19-, 18-, and 21-H), and 5.73 (1H, s, 4-H): **24**, mp 212—214 °C; MS, *m/e* 344 (M^+), 326, 311, and 301; UV, λ_{max} 245 nm (ε 17000); IR, ν_{max} 3624, 3444, 1680 (br), 1660, and 1610 cm^{-1}; NMR, δ 1.21, 1.97, and 2.25 (each 3H, s, 19-, 18-, and 21-H), 3.97 (1H, br, W_H=10 Hz, 11-H), and 5.75 (1H, s, 4-H).

References

1) Part VI, A. Murai, N. Iwasa, M. Takeda, and T. Masamune, *Bull. Chem. Soc. Jpn.*, **53**, 243 (1980).
2) Part XXXIV of "*C*-Nor-*D*-homosteroids and Related Alkaloids," Part XXXIII, Ref. 1.
3) A. Murai, H. Sasamori, and T. Masamune, *Bull. Chem. Soc. Jpn*, **51**, 234 (1978).
4) A. Murai, H. Sasamori, and T. Masamune, *Bull. Chem. Soc. Jpn.*, **50**, 437 (1977).
5) D. N. Kirk and M. P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier Publ. Co., London, (1968), p. 353.
6) A. I. Cohen, B. T. Keeler, E. J. Becker, and P. A. Diassi, *J. Org. Chem.*, **30**, 2175 (1965).
7) L. Dorfman, *Chem. Rev.*, **53**, 47 (1953).
8) E. J. Becker, R. M. Palmere, A. I. Cohen, and P. A. Diassi, *J. Org. Chem.*, **30**, 2169 (1965).
9) T. Masamune, A. Murai, K. Nishizakura, T. Orito, S. Numata, and H. Sasamori, *Bull. Chem. Soc. Jpn.*, **49**, 1622 (1976).