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Stereochemistry of the C and D Rings of *C*-Nor-*D*-homosteroids. I. The Birch Reduction of "Jervine-11β-ol" and Related Compounds

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The Birch reduction of "jervine-11β-ol" (**4**) was reinvestigated in detail. Two unknown (**6** and **7**) and two known compounds (**8** and **9**) with established configurations were newly isolated besides the previously obtained products (**2** and **5**). The main product (**2**), the C_{17} configuration of which has been left undefined, was degraded into a methyl ketone (**18**) *via* a known saturated compound (**14**) (Chart 2) or correlated with an α,β-unsaturated ketone (**23**) (Chart 3). These transformations confirmed the configuration of **2** (C_{17}–H) to be β, since the steric structures of compounds **18** and **23** have been determined in an unambiguous manner. On the other hand, the structures and configurations of **6** and **7** were elucidated as shown by the formulas on the respective spectral data as well as by hydrogenation of **6** to **14** (Chart 4) and by hydrolysis of an 11β-alcohol (**24**=**7a**), obtained by reduction of the ketone **23**, to **7** (Chart 4). These results together with those of the Birch reductions of 11-deoxojervine (**1**) and product **7** are summarized as follows: Products **2**, **6**, **7**, and **9** with the saturated 17-carbon all take the β-hydrogen configuration at C_{17}, products **3** and **5** with the C_{13}–C_{17} double bond the α-hydrogen configuration at C_{12}, and products **8** and **9** with the saturated carbons at C_{13} and C_{17} the β-hydrogen configuration at C_{12}.

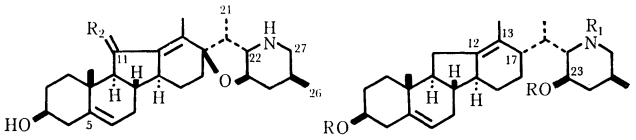
The C and D rings of *C*-nor-*D*-homosteroids show a steric behavior differing in many respects from that of normal steroids. The stereochemistry of both rings of the Birch redution products of "jervine-11β-ol" and related compounds involve several unresolved problems. We reported[1] that 11-deoxojervine (**1**) produced two diols (**2**) and (**3**) in 42 and 16% yields, respectively, and "jervine-11β-ol" (**4**) gave one (**2**) of

* Part XX of *C*-Nor-*D*-homosteroids and Related Alkaloids; Part XIX, T. Masamune and T. Orito, This Bulletin, **45**, 1888 (1972).

1) a) T. Masamune, M. Takasugi, and Y. Mori, *Tetrahedron Lett.*, **1965**, 489; b) T. Masamune, K. Kobayashi, M. Takasugi, Y. Mori, and A. Murai, *Tetrahedron*, **24**, 3461 (1968).

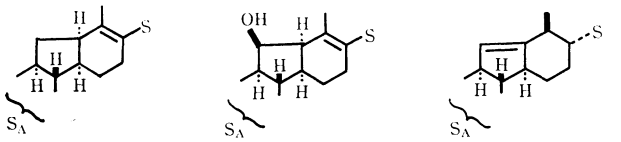
the diols and a triol (**5**) in 50 and 5% yields, respectively, by treatment with lithium in ethylamine. However, the C_{17} configuration of the main product **2** remained undefined. Compound **2** is not only an important intermediate in a series of reactions to correlate jervine and veratramine and hence to establish the C_9 configuration of jervine, but also could be a useful intermediate for skeletal transformation of the present *C*-nor-*D*-homosteroids into normal steroids.[2] Thus it became necessary to determine the configuration of **2** and improve its yield. The hydrogenation products of **2**, key substances (**14** and **15**) in the correlation in question, remained undetermined at the configurations at C_{12}, C_{13}, and C_{17}. This led us to reexamine the relevant Birch reduction of **4** and related compounds. We have isolated several compounds including **2** and **5** and elucidated their structures and configurations. The results are described in this paper.

The reduction was carried out under two different conditions; lithium and ethylamine (as in the previous work[1]) and lithium and a 5:2:2 mixture of ammonia, dioxane, and tetrahydrofuran. Three new compounds (**6**, **7**, and **8**) were isolated besides **2** and **5** under the former conditions, and two compounds (**6** and **9**) along with **2** and **5** under the latter (see Table). Compounds **5**,[1] mp 217—218 °C, **8**,[3] mp 239.5—241.5 °C, and **9**,[4] mp 234—236 °C, proved to be the known substances with established configurations. The structures and configurations of the other compounds **2**, **6**, and **7** are given in the following sections.

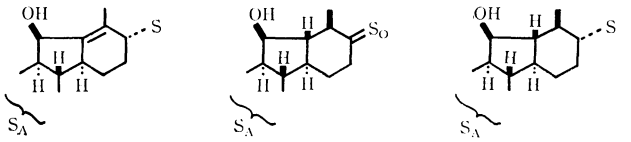


1 $R_2=H_2$
4 $R_2=$–OH,···H
Jervine $R_2=O$

2 $R=R_1=H$
2a $R=R_1=Ac$



3 $R=R_1=H$ **5** $R=R_1=H$ **6** $R=R_1=H$
6a $R=R_1=Ac$



7 $R=R_1=H$ **8** $R=R_1=H$ **9** $R=R_1=H$
7a (=**24**) $R=R_1=Ac$

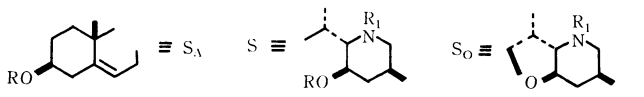


Table 1. Yields of the Birch reduction products of "jervine-11β-ol" (**4**)

Solvents	Yields (%)[a] of products					
	2a	**5**	**6a**[b]	**7**[b]	**8**[b]	**9**
$EtNH_2$	47[c]	6.1[d]	1.2	1.6	2.2	0
NH_3–dioxane–THF	72	0.06	7.5	0	0	2.4

a) Yields of isolated crystalline products.
b) New compounds.
c) Reported yield (Ref. 1b), 50% as **2**.
d) Reported yield (Ref. 1b), 5%.

Configuration at C_{17} of Compound 2. Compound **2**, mp 194.5—195.5 °C, was isolated *via* the 3-*O*,23-*O*,*N*-triacetyl derivative (**2a**), mp 195—197 °C, since it showed the same R_f value as **6**. **2** was subjected to degradation in the same way as Johnson's fragmentation;[5] namely, **2** was converted with *N*-chlorosuccinimide (NCS) into the *N*-chloro derivative, which on treatment with sodium methoxide and then with acid gave an aldehyde (**10**), ν_{max} 2710 and 1720 cm^{-1}, and τ 0.25 (1H, broad singlet, CHO) and 9.10 (3H, doublet with $J=7$ Hz, 21-Me). The aldehyde, extremely unstable in the air, was further degraded, with *n*-butyl nitrite and sodium methoxide, to an oxime (**11**), mp 161—164 °C, in 61% yield from **2**, whose NMR spectrum displayed a broad signal with $W_H=$ *ca.* 20 Hz at τ 7.04 due to the C_{17} proton. The oxime, when treated with sodium bisulfite in refluxing ethanol[6] and then with hydrochloric acid afforded a multicomponent mixture,[7] from which two products (**12**), mp 141—142.5 °C, and (**13**), mp 167.5—169 °C, were isolated in 10 and 36% yields. The former, which gave the monoacetate (**12a**), mp 119.5—120 °C, was assigned structure **12** on the basis of the mass (*m/e* 272, M^+), IR (no C=O absorption) and NMR spectra (no sharp peaks except two singlets at τ 9.04 and 8.44 due to 19- and 18-Me in the higher field, and only one C_6 olefinic proton signal at τ 4.65 in the lower field). Formation of **12** would be tentatively rationalized by assuming partial isomerization of the C_{12}–C_{13} double bond of **13** or **11** to the C_{13}–C_{17} position, hydration, retro-Claisen reaction and remigration of the resulting C_{13}–C_{17} double bond. On the other hand, the major product **13** was identified as the expected compound formed by simple hydrolysis of the oxime **11**. In accordance with the assigned structure, the mass spectrum (*m/e* 314, M^+) indicated a molecular formula $C_{21}H_{30}O_2$, and the IR and NMR spectra exhibited the presence of a C_{17} acetyl substituent (ν_{max} 1695 cm^{-1} and τ 7.91, singlet) and a 18-methyl group attached to the C_{12}–C_{13} double bond (τ 8.48, singlet). The NMR spectrum (τ 6.90, a broad signal with $W_H=$ *ca.* 23 Hz)[4] and the ORD curve (a large positive

2) *Cf.*, J. M. Coxon, M. P. Hartshown, and D. N. Kirk, *ibid.*, **21**, 2489 (1965).
3) T. Masamune, N. Sato, K. Kobayashi, I. Yamazaki, and Y. Mori, *ibid.*, **23**, 1591 (1967).
4) T. Masamune and K. Orito, *ibid.*, **25**, 4551 (1969).
5) R. W. Franck and W. S. Johnson, *Tetrahedron Lett.*, **1963**, 545; R. W. Franck, G. P. Rizzi, and W. S. Johnson, *Steroids*, **4**, 463 (1964).
6) *Cf.*, S. H. Pines, J. M. Chemerda, and M. A. Kozlowski, *J. Org. Chem.*, **31**, 3446 (1966).
7) *Cf.*, a) T. Masamune, K. Orito, and A. Murai, This Bulletin, **39**, 2503 (1966); b) S. M. Kupchan, T. Masamune, and G. W. A. Milne, *J. Org. Chem.*, **29**, 755 (1964).

Cotton effect, $a=+279°$)[8] indicated the C_{17} hydrogen to possess the β-configuration. Furthermore, on treatment of **13** with alkali in refluxing methanol, most of the starting material remained unchanged with no configurational change at C_{17}, supporting the 17β-hydrogen, while isomerization of the C_{12}–C_{13} double bond occurred only partially (less than 20%). This would be caused by serious steric interaction between 18- and 21-methyl groups with the resulting α,β-unsaturated 20-ketone.[9] However, in view of the low yield of **13** as well as of the difficult derivation of **13** to a known compound,[10] it became desirable to determine the relevant configuration more clearly. The low yield in the hydrolysis of oxime **11** was expected to be improved by saturation of the C_{12}–C_{13} double bond.

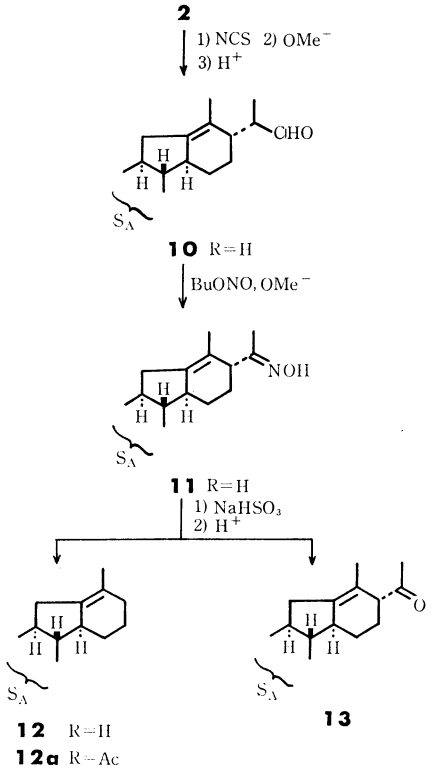


Chart 1

Hydrogenation of **2** over prereduced rhodium-platinum oxide (3:1) catalyst[11] in acetic acid proceeded smoothly, two moles of hydrogen being consumed within 1 hr, and produced a single product (**14**),[12] mp 185.5—186 °C, in 76% yield. It would be very improbable that migration of the C_{12}–C_{13} double bond occurred during the facile hydrogenation, because the same hydrogenation over only platinum required a long time (21—90 hr) for absorption of 2 mol of hydrogen and afforded a 36% yield of the isomeric compound (**15**),[13] mp 183—185 °C, along with **14**. Isomer **15** would probably be formed by migration of the C_{12}–C_{13} double bond to C_{13}–C_{17} followed by hydrogenation. While these products had already been prepared,[1] their configurations have been left undetermined. Thus, compound **14** was degraded in the same manner as **2** and converted into an oxime (**17**), mp 174—176 °C, *via* an aldehyde (**16**), amorphous, ν_{max} 2710 and 1723 cm^{-1}, and τ 0.35 (1H, singlet). Mild hydrolysis[6] of **17** afforded the corresponding methyl ketone, mp 135—137 °C, ν_{max} 1699 cm^{-1} and τ 7.89 (3H, singlet), in high yield from **14**, which proved to be identical with a known compound (**18**) with established configurations (17β-H).[14] Likewise, compound **15** was converted into the corresponding methyl ketone (**21**), mp 70—72 °C and ν_{max} 1704 cm^{-1}, in good yield, *via* an aldehyde (**19**) and an oxime (**20**). This ketone **21** displayed a broad peak with W_H=22 Hz at τ 6.40 due to the C_3 proton in the NMR spectrum, indicative of the A/B *trans*-fused linkage. It was stable against alkali (no epimerization at C_{17}) but differed from a well-defined compound (**22**)[15] prepared from jervine. On the basis of the *cis*-addition of hydrogen to double bonds[16] and the chemical shifts of 19-Me protons

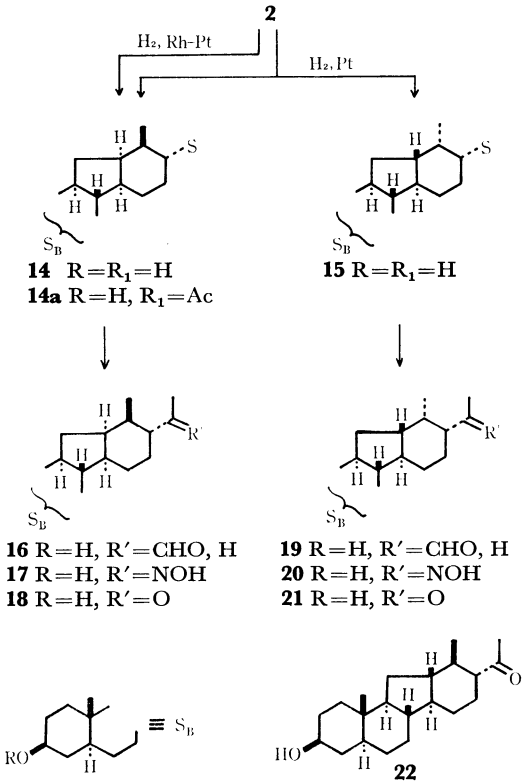


Chart 2

8) *Cf.*, K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg, and C. Djerassi, *J. Amer. Chem. Soc.*, **82**, 4740 (1960); K. Mislow and J. G. Berger, *ibid.*, **84**, 1956 (1962); K. Mislow, M. A. W. Glass, R. E. O'Brien, P. Rutkin, D. H. Steinberg, J. Weiss, and C. Djerassi, *ibid.*, **84**, 1455 (1962).

9) *Cf.*, K. G. Lewis and G. J. Williams, *Tetrahedron Lett.*, **1965**, 4573.

10) H. Mitsuhashi and K. Shibata, *Tetrahedron*, **21**, 1215 (1965).

11) S. Nishimura, This Bulletin, **33**, 566 (1960).

12) Identified as compound X in Ref. 1b, p. 3468; reported mp 185—187 °C.

13) Identified as compound X' in Ref. 1b, p. 3468; reported mp 184—186 °C.

14) a) H. Suginome, N. Sato, and T. Masamune, *Tetrahedron Lett.*, **1969**, 2671; b) N. Sato, Ph. D. Thesis, Hokkaido University, Sapporo, Japan, 1969.

15) A. Murai, T. Nishimura, and T. Masamune, unpublished results.

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

(τ 9.26, probably *trans* C/D linkage),[17] compound **15** would possibly be formulated as structure **15**. Thus, these findings confirmed the conclusion (17β-H) in the preceding section.

Further confirmation could be obtained by correlating **2** with a compound (**23**)[18] with unambiguous configurations,[4] prepared readily from jervine by a three-step process. Reduction of **23** with sodium borohydride in refluxing dioxane followed by acetylation of the product afforded a multi-component mixture, from which three compounds were isolated by preparative tlc. One, mp 213—215 °C, isolated in 14% yield, could be assigned to formula **24** on the spectral data, ν_{max} 3570 cm^{-1} and τ 8.74 (singlet, 19-Me)[17] and 8.23 (singlet, 18-Me). Compound **24** was converted by oxidation with chromic anhydride in pyridine into the original ketone **23a**, indicative of retention of the C_{17} configuration during the course of sodium borohydride reduction. Treatment of **24** with lithium in ethylamine and subsequent acetylation resulted in formation of **2a** in 74% yield, establishing the configuration in question to be β. Incidentally, the other two compounds resisted crystallization, but mild hydrolysis effected formation of two crystalline *N*-acetyl compounds, mp 248—251 °C and 241—242 °C. These could be inferred to possess structures **25** and **26**, but were not further examined.

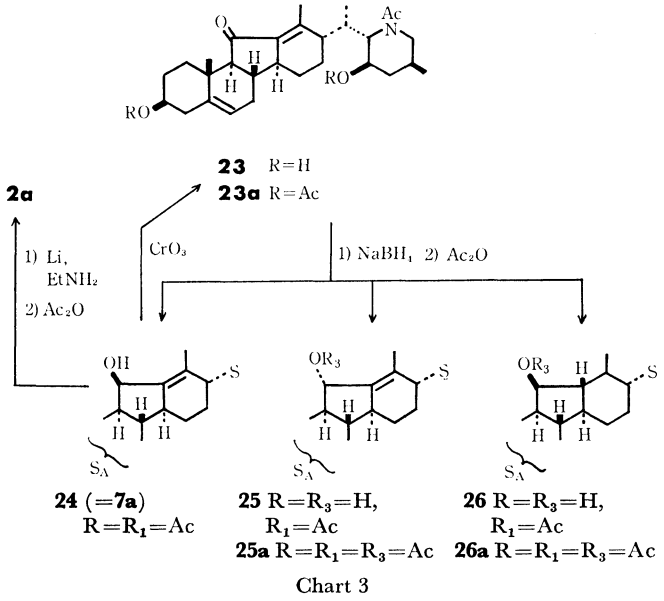


Chart 3

Structure and Configuration of Compound **6**. This compound could be isolated as the 3-*O*,23-*O*,*N*-triacetyl derivative (**6a**), mp 173—174 °C, which on hydrolysis gave **6**, mp 229—231.5 °C. Compound **6a**, $C_{33}H_{49}O_5N$, exhibited a parent peak at *m/e* 539 and a broad singlet with W_H=9 Hz at τ 4.62 due to two olefinic protons in the mass and NMR spectra. These indicated the compound to be an isomer of **2a** and to be formulated most favorably as structure **6a**. In fact, **6a** was produced by a modification of the Huang-Minlon procedure[19] for the Wolff-Kishner reduction of **23** followed by acetylation in 45% yield along with **2a** (30%), and also obtained by treatment of **24** with lithium in a 5:2:2 mixture of ammonia–dioxane–tetrahydrofuran and subsequent acetylation in 12% yield. The reduction of **24** with lithium in ethylamine gave no detectable amount of **6**. These transformations confirmed not only a planar structure of **6** but also the β-configuration at C_{17}. On the other hand, hydrogenation of **6a** over rhodium-platinum[11] in acetic acid for 2 hr led to saturation of the compound and, after hydrolysis, formation of the *N*-acetyl compound, mp 180—182 °C and ν_{max} 1641 cm^{-1}, which was identical with a compound (**14a**), mp 180.5—182.5 °C, obtained by triacetylation of **14** followed by partial hydrolysis. These results indicate that the hydrogen at C_{13} possesses α-configuration, since migration of the C_{11}–C_{12} double bond would be very improbable during the course of hydrogenation. On the basis of these configurational assignments, the Wolff-Kishner reduction would be rationalized by assuming that it proceeds by path B[20] (Chart 4) and is completed by axial approach of the proton source to the C_{13}, as elaborated by Zimmerman[21] in many examples of reketonization of enols.

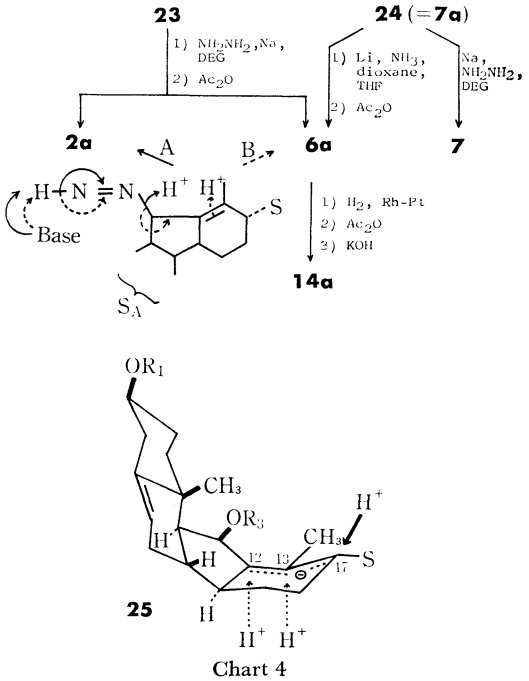


Chart 4

Structure and Configuration of Compound **7**. The compound was analyzed for $C_{27}H_{43}O_3N$ and showed peaks at *m/e* 429, 141, and 114 in the mass spectrum. The spectrum not only supported the molecular formula but also indicated cleavage of the C_{17}–O ether bond,

17) T. Masamune, *Nippon Kagaku Zasshi*, **91**, 407 (1970).

18) T. Masamune, M. Takasugi, M. Gohda, H. Suzuki, S. Kawahara, and T. Irie, *J. Org. Chem.*, **29**, 2282 (1964).

19) *Cf.*, D. H. R. Barton, D. A. J. Ives, and B. Thomas, *J. Chem. Soc.*, **1956**, 2056.

20) a) T. Masamune, Y. Mori, M. Takasugi, and A. Murai, *Tetrahedron Lett.*, **1964**, 913; b) T. Masamune, Y. Mori, M.Takasugi, A. Murai, S. Ohuchi, N. Sato, and N. Katsui, This Bulletin, **38**, 1374 (1965).

21) H. E. Zimmerman and A. Mais, *J. Amer. Chem. Soc.*, **81**, 4305 (1956), and their previous papers.

suggesting formula **7**. Thus **24** was hydrolyzed for 17 hr under the conditions of a modified Huang-Minlon procedure.[19] The product was identical with **7**, confirming the structure and configuration of compound **7**.

Summary of Results. The results of the Birch reduction of **4** and **7a** (=**24**), together with those of **1**,[1] are summarized as follows. Apart from compound **8**, all C_{17}-saturated compounds **2**, **6**, **7**, and **9** take the β-hydrogen configuration at C_{17}, while compounds **3** and **5** with the C_{13}–C_{17} double bond possess the α-hydrogen at C_{12}. As shown with simpler model compounds,[22] these results would probably be caused by the continued maximum overlap[21,23] between the π-orbitals at C_{12}, C_{13}, and C_{17} of reduction carbanion intermediates such as **25**, on approach of the proton sources.[22] It is to be noted that saturated compounds **8** and **9** were formed, resulting from reduction of isolated double bonds under the Birch conditions. Moreover, the fact that **8** and **9** adopt the β-hydrogen configuration at C_{12} can be well interpreted, considering the results of the Birch reduction[4] of **23** as well as *trans*-hydrogenation[16] of jervine over platinum in acetic acid leading to the corresponding 12β,13α-dihydro compounds, since protonation at C_{12} of the respective reaction intermediates, C_{12}–C_{13} anion radical or dianion formed from **4** *via* the relevant double bond and 11-en-11-ol or 11-en-11-olate from **23** and jervine, wound proceed in the same manner as reketonization of enols.[21]

Experimental

All the mps were measured in sealed capillaries and uncorrected. The homogenity of each compound was always checked by tlc on silica gel (Wakogel B-5) using various solvent systems, and the spots were developed with ceric sulfate in dil. sulfuric acid and/or iodine. The optical rotations, ORD curves, and IR spectra were measured in chloroform, methanol, and Nujol, respectively, unless otherwise stated. The NMR spectra were obtained in deuterochloroform at 60 and/or 100 MHz, and the chemical shifts were given in τ-values, TMS being used as an internal reference. Abbreviations "s, d, t, m, br, and sh" in the NMR and IR spectra denote "singlet, doublet, triplet, multiplet, broad and shoulder," respectively.

Birch Reduction of "Jervine-11β-ol" (4) with Lithium in Ethylamine (cf. Ref 1b). To **4** (800 mg) dissolved in refluxing anhydrous ethylamine (31 ml) was added finely divided lithium metal (647 mg), and the mixture was refluxed under vigorous stirring for 2.5 hr. After addition of ammonium chloride, the mixture was warmed to remove the solvent, and the residue mixed with water (50 ml) and extracted with chloroform repeatedly. The chloroform solution was washed with water, dried with anhydrous sodium sulfate and evaporated to leave amorphous residue (974 mg), which showed 5 spots on tlc and was separated by preparative tlc, using a 10: 1 mixture of ether and methanol and 46 plates; each was made of silica gel (Wakogel B-5, 10 g) with an area of 20 cm by 20 cm.

Each fraction was extracted with methanol, and the solution evaporated below 50 °C. The residue was again dissolved in chloroform, washed with a 5% sodium bicarbonate solution and water, treated with active charcoal, dried and evaporated. The most mobile fraction (90 mg), amorphous, showed a parent peak at *m/e* 413 in the mass spectrum but was not further examined. The second fraction (502 mg) was treated with acetic anhydride (11 ml) and pyridine (11 ml) at room temperature for 17 hr. After removal of the solvents, the residue was treated with water and chloroform, and the chloroform solution was washed with 1M hydrochloric acid, a 5% sodium bicarbonate solution and water, dried and evaporated to leave amorphous substance (733 mg), which partially crystallized on trituration with aqueous methanol. The crystalline material was collected by filtration and recrystallized from the same solvent to give 3-*O*,23-*O*,*N*-triacetyl-22,27-imino-17β-jerva-5,12-diene-3β,23β-diol (**2a**, 400 mg), mp 195—197 °C (lit,[1b] 188—190 °C); $[\alpha]_D$ −48.0° (lit,[1b] −12.3° in 95% EtOH); mass, *m/e* 539 (M^+); IR, ν_{max} 1738, 1625, 1239 and 1025 cm^{-1}; NMR τ 9.23 and 8.84 (each 3H, d, J=6.5 and 7 Hz, 21- and 26-Me or *vice versa*), 9.05 (3H, s, 19-Me), 8.50 (3H, s, 18-Me), 7.99 (6H, s, $OCOC\underline{H}_3$), and 7.89 (3H, s, $NCOC\underline{H}_3$) (*cf.*, Ref 1b). On the other hand, the filtrate was evaporated and then separated into two parts by preparative tlc(ether–benzene 1: 2, and 18 plates). Each acetone eluate was worked up as mentioned above, and the more mobile fraction (41 mg) crystallized on trituration with isopropyl ether and was recrystallized to yield 3-*O*,23-*O*,*N*-triacetyl-22,27-imino-17β-jerva-5,11-diene-3β,23β-diol (**6a**, 12 mg), mp 173—174 °C; $[\alpha]_D$ −28.5°; mass, *m/e* 539 (M^+); IR, ν_{max} 1740, 1637, 1240, 1040, and 1025 cm^{-1}; NMR, τ 9.04 (3H, s, 19-Me), and 4.63 (2H, br s W_H=9 Hz, H at C_6 and C_{11}).

Found: C, 73.22; H, 9.34; N, 2.26%. Calcd for $C_{33}H_{49}O_5N$: C, 73.43; H, 9.15; N, 2.60%.

The less mobile fraction (135 mg) crystallized from aqueous methanol, (77 mg), mp 191—194 °C, and was identical with **2a**.

The third, middle fraction (104 mg) was crystallized and recrystallized from methanol–acetone to give 22,27-iminojerva-5,13(17)-diene-3β,11β,23β-triol (**5**, 49 mg), mp 217—218 °C, which was identical with an authentic sample.[1b]

The fourth fraction (62 mg) crystallized on trituration from methanol–acetone, mp 221—225 °C, and was recrystallized from the same solvent to yield 22,27-imino-17β-jerva-5,12-diene-3β,11β,23β-triol (**7**, 13 mg), mp 228—231 °C, which was identical with a compound prepared by hydrolysis of **24** (=**7a**), described later; IR, ν_{max} 3420 and 1046 cm^{-1}.

The least mobile fraction (31 mg) crystallized on trituration with methanol–acetone, mp 235—236 °C, and was recrystallized from the same solvent to afford 22,27-imino-17β,23β-oxidojerv-5-ene-3β,11β-diol (**8**, 17.5 mg), mp 239.5—241.5 °C, which was identical with an authentic specimen.[3]

Birch Reduction of 4 with Lithium and a Mixture of Ammonia, Dioxane, and Tetrahydrofuran (THF). To a suspended mixture of **4** (800 mg) in liquid ammonia (200 ml), dry dioxane (80 ml) and dry THF (80 ml) was added lithium (565 mg), and the mixture was stirred vigorously under reflux for 1 hr. To the refluxing mixture was added dropwise dry ethanol (7.2 ml) for 4 min, when the blue color disappeared. After addition of lithium (315 mg), the mixture was again refluxed under stirring for 15 min and, on addition of dry ethanol (4 ml) for 2 min, became colorless again. After removal of the ammonia, the solvents were evaporated below 50 °C, and the residue was mixed with water (50 ml) and extracted with chloroform repeatedly. The chloroform solution was worked up as mentioned above to give crystalline residue (812 mg), showing 5 spots on tlc. Fractional recrystallizations from

22) T. Masamune, H. Matsue, and M. Fujii, This Bulletin, **45**, 1812 (1972).

23) G. Stork and S. D. Darling, *J. Amer. Chem. Soc.*, **86**, 1761 (1964).

methanol–acetone afforded crystalline material (489 mg), which showed a single spot corresponding to the second fraction in the preceding reduction (run a). All mother liquors were combined and separated into 5 parts by preparative tlc, using a 10: 1 mixture of ether and methanol and 31 plates. The most mobile fraction (14 mg), amorphous, was identical with the corresponding one in run a.

The second fraction (255 mg) was combined with the afore-mentioned crystalline material and acetylated with acetic anhydride (13 ml) and pyridine (13 ml) at room temperature overnight. The product (1018 mg), showing two spots, crystallized on trituration with aqueous methanol and, on recrystallization from the solvent, afforded **2a** (666 mg), mp 192—194 °C. The filtrates were combined and separated by preparative tlc (ether–benzene 1: 2, and 19 plates) and worked up as in run a. The more mobile fraction (109 mg) afforded **6a** (76 mg), mp 168—170 °C (from isopropyl ether), and the less mobile (113 mg) **2a** (62 mg), mp 193—195 °C (from aqueous methanol).

The middle fraction (7 mg) crystallized on trituration with methanol–acetone and was recrystallized from the same solvent to give **5** (0.5 mg), mp 214—215 °C, which was identical with sample **5** in run a in the mass spectrum and R_f value on tlc.

The fourth fraction (41 mg) crystallized on trituration with methanol–acetone (19 mg), mp 234—236 °C.

Recrystallization from the same solvent afforded 22,27-imino-17β-jerv-5-ene-3β,11β,23β-triol (**9**), which was identical with an authentic sample.[4]

The last fraction (19 mg) crystallized on trituration with methanol–acetone, (11 mg) mp 179—180 °C, but was not further examined.

Compound **2a** was hydrolyzed as follows. To diethylene glycol (DEG) (100 ml) with dissolving sodium (3 g) was added anhydrous hydrazine (20 ml), and the solution was refluxed for 30 min. After addition of **2a** (2.06 g), the whole solution was refluxed for 21 hr and then cooled, when the condenser was replaced by a distillation apparatus. The solution was again heated for 30 min, evaporating off the hydrazine, cooled and poured into ice-water (one l), when precipitates separated and were collected by filtration, washed with water repeatedly and dissolved in methanol. The methanol solution was evaporated to leave amorphous substance, which crystallized on trituration with acetone (1.45 g), mp 194—194.5 °C. This was recrystallized for analysis to give **2**, mp 194.5—195.5 °C (lit,[1b] 193—195 °C); $[\alpha]_D$ −70.6° (MeOH) (lit,[1b] −61° in 95% EtOH); mass, *m/e* 413 (M^+); IR, ν_{max} 3385, 3105, 1063, 1039, 888, and 812 cm^{-1}.

Found: C, 78.15; H, 10.51; N, 3.33%. Calcd for $C_{27}H_{43}O_2N$: C, 78.40; H, 10.48; N, 3.39%.

Compound **6a** (101 mg) was hydrolyzed in the same manner as **2a**, using DEG (5 ml), sodium (200 mg), and hydrazine (1 ml). The product crystallized on trituration with acetone, (66 mg), mp 228—229 °C. This was recrystallized for analysis to give **6**, mp 229—231.5 °C; $[\alpha]_D$ −85.0° (MeOH); mass, *m/e* 413 (M^+); IR, ν_{max} 3390, 3130, 1079, 1068, 1039, 890, and 812 cm^{-1}.

Found: C, 77.97; H, 10.46; N, 3.41%. Calcd for $C_{27}H_{43}O_2N$: C, 78.40; H, 10.48; N, 3.39%.

*17α-Acetyletiojerva-5,12-dien-3β-ol 20-oxime (**11**).* To a solution of **2** (5.0 g) in dry THF (250 ml) was added *N*-chlorosuccinimide (NCS) (2.0 g), and the mixture was stirred at room temperature for 2 hr. After removal of the solvent below 28 °C, the residue was mixed with methanol (150 ml). To the suspended mixture was added 2M sodium methoxide in methanol (150 ml) under cooling with an ice-bath in a stream of nitrogen. The mixture was stirred at room temperature for 4.5 hr, when the mixture became homogeneous, and then evaporated below 45 °C. The residue was mixed with water and then with 6M hydrochloric acid (100 ml) under cooling, stirred vigorously at room temperature overnight and filtered. The precipitates were dissolved in chloroform, and the chloroform solution washed with 1M hydrochloric acid, a 5% sodium bicarbonate solution and water, dried and evaporated below 27 °C to leave amorphous 20-aldehyde (**10**, 4.0 g), which showed a single spot; mass, *m/e* 328 (M^+) and 270 (M^+–side chain, CH_3CHCHO); IR, ν_{max} 3600, 3450, 2710, 1720, and 1047 cm^{-1}; NMR, τ 9.10 (3H, d J=7 Hz, 21-Me), 9.01 (3H, s, 19-Me), 8.42 (3H, s, 18-Me), 6.45 (1H, m W_H=26 Hz, H at C_3), 4.65 (1H, br a W_H=9 Hz, H at C_6), and 0.25 (1H, s, CHO).

To a cooled solution of **10** (1.06 g) in methanol (50 ml) were added *n*-butyl nitrite (6 ml) and 1.7M sodium methoxide in methanol (50 ml) under nitrogen, and the solution was allowed to stand in a refrigerator (6 °C) for 14 hr. After removal of the solvents below 39 °C, the residue was mixed with water (30 ml) and acidified to pH 3 by dropwise addition of 6M hydrochloric acid (15 ml) under cooling and stirring, and then extracted with chloroform. The chloroform solution was washed with a 5% sodium bicarbonate solution, dried and evaporated below 30 °C to leave oil, which was purified by preparative tlc (ether–benzene 1: 1, and 35 plates). The main fraction, acetone eluate, was evaporated and redissolved in chloroform, and the solution gave amorphous substance (650 mg), which crystallized on trituration with methanol–isopropyl ether, mp 148—151 °C. Recrystallization from the same solvent afforded an analytical sample of 20-oxime (**11**), mp 161—164 °C; $[\alpha]_D$ +37.3°; IR, ν_{max} 3435, 3255, 1660, and 1054 cm^{-1}; NMR, τ 9.03 (3H, s, 19-Me), 8.53 (3H, s, 18-Me), 8.29 (3H, s, 21-Me), 7.04 (1H, br W_H=20 Hz, H at C_{17}), 6.50 (1H, br W_H=28 Hz, H at C_3), and 4.62 (1H br s, W_H=9 Hz, H at C_6).

Found: C, 76.77; H, 9.85; N, 3.76%. Calcd for $C_{21}H_{31}O_2N$: C, 76.55; H, 9.48; N, 4.25%.

*Etiojerva-5,12-dien-3β-ol (**12**) and 17α-Acetyletiojerva-5,12-dien-3β-ol (**13**).* A solution of **11** (650 mg) in ethanol (35 ml) and water (24.5 ml) containing sodium bisulfite (1.36 g) was refluxed under stirring for 13 hr.[6] After removal of the solvents, the residue was stirred vigorously with 1M hydrochloric acid (70 ml) and chloroform (70 ml) at room temperature for 2 hr. After separation of the chloroform layer, the aqueous solution was extracted with chloroform repeatedly. All the chloroform solutions were combined, washed with 1M hydrochloric acid, a 5% sodium bicarbonate solution and water, dried and evaporated to give amorphous residue (390 mg), showing 6 spots, which was separated by preparative tlc (ether–benzene 1: 2, and 21 plates).

The first, most mobile fraction (66 mg) crystallized on trituration with acetone–isopropyl ether (53 mg), mp 138—139 °C. Recrystallization from isopropyl ether afforded an analytical sample of **12**, mp 141—142.5 °C; $[\alpha]_D$ −68.3°; mass, *m/e* 272 (M^+); IR, ν_{max} 3250 and 1058 cm^{-1} (no C–O absorption); NMR, τ 9.04 (3H, s, 19-Me), 8.44 (3H, s, 18-Me), 8.39 (1H, s, OH, checked by addition of D_2O), 6.47 (1H, br W_H=24 Hz, H at C_3), and 4.65 (1H, br s W_H= 10 Hz, H at C_6).

Found: C, 84.02; H, 9.99%. Calcd for $C_{19}H_{28}O$: C, 83.77; H, 10.36%.

Compound **12** (47 mg) was acetylated with acetic anhydride (1 ml) and pyridine (1 ml) at room temperature overnight. After being worked up as usual, the mixture gave crystalline substance (47 mg), which was recrystallized from aqueous acetone to give the monoacetate (**12a**, 27 mg), mp 114—117.5 °C. This was recrystallized from the same solvent for analysis;

mp 119.5—120 °C; $[\alpha]_D$ −83.9°; mass, *m/e* 254 (M^+–AcOH); IR, ν_{max} 1727, 1241 and 1030 (no OH absorption); NMR, τ 9.03 (3H, s, 19-Me); 8.44 (3H, s, 18-Me), 7.96 (3H, s, OCOCH$_3$), 5.39 (1H, septet J=4 Hz, H at C_3), and 4.61 (1H, br s W_H=12 Hz, H at C_6).

Found: C, 80.05; H, 9.48%. Calcd for $C_{21}H_{30}O_2$; C, 80.21; H, 9.62%.

The second, main fraction (223 mg), crystalline, was recrystallized from acetone–isopropyl ether to yield **13** (198 mg), mp 167.5—168 °C. This was recrystallized from the same solvent for analysis; mp 167.5—169 °C; $[\alpha]_D$ +68.2°; ORD, $[\phi]_{311}^{peak}$ +120°, $[\phi]_{287}$ 0°, $[\phi]_{259}^{trough}$ −159°, a=+279°; mass, *m/e* 314 (M^+); IR, ν_{max} 3456, 1695, and 1065 cm^{-1}; NMR, τ 9.03 (3H, s, 19-Me), 8.48 (3H, s, 18-Me), 8.17 (1H, s, OH, checked by addition of D_2O), 7.91 (3H, s, 21-Me), 6.90 (1H, br W_H=23 Hz, H at C_{17}), 6.48 (1H, br W_H=23 Hz, H at C_3), and 4.64 (1H, br s W_H=9 Hz, H at C_6).
Found: C, 80.46; H, 9.43%. Calcd for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%.

The third fraction (40 mg), oil, was a mixture of two products having almost the same R_f values; IR ($CHCl_3$), ν_{max} 1644 and 1047 cm^{-1}. Each of the fourth (13 mg) and last (13 mg) fractions showed a single spot on tlc and no C=O absorption maxima. None of these fractions were further examined.

Compound **13** (47 mg) was treated with 5% potassium hydroxide in refluxing methanol (20 ml) for 17 hr under nitrogen. After removal of the solvent, the residue was treated with water and chloroform, and the chloroform solution gave amorphous product (57 mg), showing 2 spots. This was separated by preparative tlc (ether–benzene 1:2, and 3 plates). The main, more mobile crystalline fraction (30 mg), showing practically the same IR spectrum as **13**, was recrystallized from acetone–isopropyl ether to give the starting material (10 mg), mp 164—165 °C. The less mobile fraction (7.5 mg), oil, resisted crystallization and showed the following IR and NMR spectra, but was not further examined; IR ($CHCl_3$), ν_{max} 3580, 3450, 1706, 1644, and 1047 cm^{-1}; NMR, τ 8.98 (3H, s), 8.82 (3H, s), 8.29 (s, OH, checked by addition of D_2O), 7.97 (3H, s, 21-Me), 6.45 (1H, br W_H=25 Hz, H at C_3), and 4.64 (1H, br s W_H=11 Hz, H at C_6). This might be a 13ξ-hydroxyetiojervane derivative with a C/D *cis*-fused linkage.

Hydrogenation of **2**. *22,27-Imino-5α,12α,17β-jervane-3β,23β-diol (**14**) and 22,27-imino-5α,13β,17β-jervane-3β,23β-diol (**15**).*
a) A suspended, 3:1 mixture of rhodium and platinum oxide[11] (1.017 g) in acetic acid (20 ml) was prereduced with hydrogen for 2.7 hr, when 281 ml of hydrogen had been consumed. Compound **2** (2.501 g) in acetic acid (40 ml) was added to the mixture and then hydrogenated for 1 hr, when 286 ml of hydrogen (2.0 mol) had been absorbed. The reaction was further continued for 48 hr but without absorption of hydrogen and, after addition of the prereduced catalyst (217 mg) freshly prepared, for another 24 hr, when only 0.18 mol of hydrogen had been consumed. After filtration of the catalyst and subsequent evaporation of the acetic acid below 67 °C, the residue was mixed with water (10 ml), cooled, basified with 6M ammonium hydroxide (20 ml) to pH over 11, and mixed with chloroform (35 ml). The whole mixture was stirred vigorously at room temperature for 20 hr, when chloroform-addition compounds (3.83 g) remaining suspended between the aqueous and chloroform layers were collected by filtration and dissolved in methanol. The solution was evaporated to leave amorphous residue (2.266 g), showing a single spot, which crystallized on trituration with methanol–acetone (1:1) and was collected by filtration to yield **14** (1.905 g), mp 182.5—184.5 °C. This was identical with compound X[1b] obtained already, and recrystallized from the same solvent for analysis; mp 185.5—186 °C (lit,[1b] 185—187 °C); $[\alpha]_D$ −52.9° (MeOH) (lit,[1b] −28.5° in 95% EtOH); mass, *m/e* 417 (M^+) and 114; IR, ν_{max} 3400, 3285, and 1041 cm^{-1}.

Found: C, 77.68; H, 11.40; N, 3.29%. Calcd for $C_{27}H_{47}O_2N$; C, 77.64; H, 11.34; N, 3.35%.

Compound **14** (102 mg) was heated with acetic anhydride (2 ml) and pyridine (2 ml) at 90 °C for 2 hr. After removal of the solvents by azeotropization with benzene, the residue was refluxed with 5% potassium hydroxide in methanol (10 ml) for 1 hr. The reaction mixture was evaporated and mixed with water, when white precipitates separated out and were collected by filtration. These were washed with water, dried and dissolved in ethyl acetate. On being allowed to stand, the solution gave crystalline material (109 mg), mp 180—181 °C. This was recrystallized from ethyl acetate to give an analytical sample of the *N*-acetyl derivative (**14a**) of **14**, mp 180.5—182.5 °C; $[\alpha]_D$ −10.1° (MeOH); mass, *m/e* 459 (M^+) and 156; IR, ν_{max} 3285, 1641, 1611, 1041, 1030 (sh), and 1023 cm^{-1}; NMR, τ 9.26 (3H, s, 19-Me).

Found: C, 75.61; H, 10.61; N, 2.99%. Calcd for $C_{29}H_{49}O_3N$: C, 75.77; H, 10.64; N, 3.05%.

b) Compound **2** was hydrogenated over platinum in almost the same manner as reported;[1b] **2** (2.50 g) was reduced over prereduced platinum oxide (1.0 g) in acetic acid (55 ml) at room temperature for 47 hr, when 1.6 mol of hydrogen had been absorbed. The reaction was continued for another 47 hr after addition of the catalyst (0.55 g), and 2.1 mol of hydrogen was consumed in all. The mixture was worked up as usual and the product was separated into a chloroform-addition compound (**14**) and a chloroform-soluble fraction. The latter crystallized on trituration with acetone and was recrystallized to give **15**, mp 180—182 °C, which was identical with compound X′ obtained already.[1b] This was recrystallized from acetone for analysis; mp 183—185 °C (lit,[1b] 184—186 °C); $[\alpha]_D$ −7.8°; IR, ν_{max} 3270, 1056, and 1029 cm^{-1}; NMR, τ 9.26 (3H, s, 19-Me).

Found: C, 77.46; H, 11.57; N, 3.24%. Calcd for $C_{27}H_{47}O_2N$: C, 77.64; H, 11.34; N, 3.35%.

*17α-Acetyl-5α,12α-etiojervan-3β-ol 20-Oxime (**17**).* A solution of **14** (1.843 g) in THF (80 ml) was stirred with NCS (722 mg) at room temperature for 1.8 hr and, after removal of the solvent below 27 °C, the residue was dissolved in chloroform (200 ml). The solution was washed with water (3×55 ml), dried and evaporated to leave amorphous residue (2.383 g) after being dried over phosphorus pentoxide. To the cooled residue in methanol (50 ml) was added 2M sodium methoxide in methanol (50 ml) under nitrogen, and the solution was stirred for 2 hr and then concentrated to 20 ml below 35 °C for 50 min. The concentrate was mixed with 6M hydrochloric acid (50 ml) and water (200 ml) under cooling, stirred at room temperature overnight, and then extracted with chloform (4×50 ml). The chloroform solution was washed with water, dried and evaporated below 35 °C to give amorphous 20-aldehyde (**16**, 1.541 g), showing a single spot; IR ($CHCl_3$), ν_{max} 3605, 3420, 2710, 1723, 1067, and 1033 cm^{-1}; NMR, τ 9.20 (3H, s, 19-Me), 9.12 and 9.00 (each 3H, d J=7 Hz, 18- and 21-Me or *vice versa*), 6.39 (1H, m W_H=19 Hz, H at C_3), and 0.35 (1H, s, CHO).

A solution of **16** (1.492 g) in methanol (70 ml) was treated with *n*-butyl nitrite (6 ml) and sodium methoxide, prepared from sodium (2.9 g) and methanol (70 ml), in a refrigerator (0 °C) for 14 hr, acidified to pH 6.0 with concd hydrochloric acid (10.5 ml) under cooling, and allowed to stand for 1 hr. The whole mixture was shaken with water (100 ml) and chloroform (3×100 ml), and the chloroform solution gave

oily residue (1.671 g), which showed a single spot but resisted crystallization; IR ($CHCl_3$), ν_{max} 3600 (BuOH), 3300, 1651, 1066, and 1030 cm^{-1}. A part (45.5 mg) of the residue was purified by preparative tlc (ether–benzene 1:1, and 2 plates). The main fraction was extracted with acetone, and the solution gave crystalline material (32.7 mg), which was recrystallized from acetone–isopropyl ether to yield **17** (24 mg), mp 174—176 °C; $[\alpha]_D$ −80.3°; IR, ν_{max} 3650, 3410, 3250, 1643, 1065, 1036, and 1014 cm^{-1}.

Found: C, 75.55; H, 10.61, N, 4.45%. Calcd for $C_{21}H_{35}O_2N$: C, 75.63; H, 10.58; N, 4.20%.

17α-Acetyl-5α,12α-etiojervan-3β-ol (18). A solution of **17** (1.619 g in crude state) in ethanol (100 ml) and water (67 ml) was refluxed with sodium bisulfite (2.1 g) for 11 hr under stirring.[6] The solution was concentrated to 20 ml, cooled, mixed with 1M hydrochloric acid (64 ml) and chloroform (96 ml), and the mixture was stirred vigorously at room temperature for 2 hr. The organic layer was combined with chloroform washings of the aqueous layer, washed with water, dried and evaporated below 35 °C to leave amorphous residue (1.335 g), which crystallized on trituration with acetone and was collected by filtration to give **18** (825 mg), mp 133—135 °C. This was recrystallized from aqueous methanol for analysis; mp 135—137 °C; $[\alpha]_D$ −54.6°; IR, ν_{max} 3460, 1699, 1066, and 1041 cm^{-1}; NMR, τ 9.20 (3H, s, 19-Me), 9.18 (3H, d J=5.5 Hz, 18-Me), 7.89 (3H, s, 21-Me), and 6.40 (1H, m W_H=25 Hz, H at C_3). The afore-mentioned filtrate on crystallization was subjected to preparative tlc (ether–benzene 1:1, and 23 plates), and the main fraction extracted with acetone and then with methanol afforded amorphous substance (352 mg), which on trituration with acetone afforded an additional amount of **18** (168 mg), mp 129—134 °C. Compound **18** proved to be identical with an authentic sample already reported[14b] (the acetate[14a]) by direct comparison.

Compound **18** (30 mg) was treated with 1M sodium methoxide in refluxing methanol (20 ml) for 12 hr under nitrogen. The reaction mixture was worked up as usual and gave crystalline material (31 mg), which showed the same IR spectrum and R_f value on tlc as the starting material, and was recrystallized from aqueous methanol to yield **18** (20 mg), mp 135—136 °C; $[\alpha]_D$ −51.7°.

17α-Acetyl-5α,13β-etiojervan-3β-ol (21). Compound **15** was degraded into the corresponding methyl ketone (**21**) in the same manner as **14**. A solution of **15** (810 mg) in THF (30 ml) was converted into the *N*-chloro derivative by treatment with NCS (400 mg) for 1.7 hr. This in methanol (50 ml), on treatment with 2 M sodium methoxide in methanol (50 ml) under cooling for 3 hr followed by hydrolysis of the product with 2M hydrochloric acid at room temperature for 69 hr, produced crude 20-aldehyde (**19**, 786 mg), which on purification by preparative tlc (ether–benzene 1:1 and 36 plates) gave **19** (374 mg), amorphous; IR ($CHCl_3$), ν_{max} 3590, 3420, 2780, 1724, and 1028 cm^{-1}; NMR, τ 9.25 (3H, s, 19-Me), 9.04 and 9.03 (total 6H, each d J=7 and 5 Hz, 18- and 21-Me or *vice versa*), 6.46 (1H, br W_H=30 Hz, H at C_3), and 0.40 (1H, s, CHO).

20-Aldehyde (**19**, 270 mg) in methanol (15 ml) was treated with *n*-butyl nitrite (1.2 ml) and 1.3M sodium methoxide in methanol (20 ml) at 0 °C for 11 hr to yield 20-oxime (**20**, 334 mg), showing a single spot; IR ($CHCl_3$), ν_{max} 3600, 3280, and 1027 cm^{-1} (no C=O absorption). A solution of **20** (315 mg) in 40% aqueous ethanol was refluxed with sodium bisulfite for 10 hr[6] and, after removal of the solvent, stirred with 1M hydrochloric acid (9 ml) and chloroform (15 ml) at room temperature for 1.5 hr to give amorphous residue (278 mg). This was subjected to preparative tlc (ether–benzene 1:2, and 13 plates) and gave amorphous substance (**21**, 133 mg) as the main fraction, showing the same IR spectrum and R_f value as the analytical sample described below, which crystallized on trituration with acetone–*n*-hexane to yield **21** (41 mg), mp 70—72 °C; $[\alpha]_D$ +15.4°; IR ($CHCl_3$), ν_{max} 3600, 3435, 1704, and 1027 cm^{-1}; NMR, τ 9.26 (3H, s, 19-Me), 9.17 (3H, d J=6 Hz, 18-Me), 7.90 (3H, s, 21-Me), and 6.40 (1H, br W_H=22 Hz, H at C_3).

Found: C, 79.24; H, 10.58%. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76%.

Compound **21** (17 mg) was treated with 1M sodium methoxide in refluxing methanol for 12 hr, and the product (14 mg), amorphous, showed the same IR spectrum and R_f value on tlc as the starting material.

Reduction of N-*acetyl-22,27-imino-17β-jerva-5,12-diene-3β,23β-diol-11-one (23) with sodium borohydride. 3-O,23-O,N-Triacetyl-22,27-imino-17β-jerva-5,12-diene-3β,11β,23β-triol (24=7a) and Others (25 and 26).* A solution of **23**[16,18] (1.5 g) in dioxane (150 ml) was refluxed with sodium borohydride (NBH) (3.0 g) under stirring for 48 hr. After addition of acetone under cooling to decompose excess NBH, the mixture was further stirred for 15 min, insoluble material being filtered off. The filtrate was evaporated, shaken with water and chloroform. The chloroform solution afforded amorphous residue (1.71 g), which showed 2 spots on tlc; IR ($CHCl_3$), ν_{max} 3590, 3410, 1641, 1048 and 1020 cm^{-1} (no C=O absorption). A part (1.67 g) of the residue was acetylated with acetic anhydride (15 ml) and pyridine (15 ml) at room temperature for 21 hr. After being worked up in the usual way, the mixture gave amorphous residue, which was separated into 3 parts by preparative tlc (ether–benzene 1:1, and 62 plates). The most mobile fraction (**25a**, 535 mg), amorphous, resisted crystallization; NMR, τ 9.18 and 8.81 (each 3H, d J=6 and 5 Hz, 21- and 26-Me or *vice versa*), 8.89 (3H, s, 19-Me), 8.50 (3H, s, 18-Me), 8.00 (9H, s, OCOCH_3), and 7.88 (3H, s, NCOCH_3). This was then hydrolyzed with 5% potassium hydroxide in refluxing methanol (50 ml) for 1 hr under nitrogen, and gave amorphous substance, which crystallized on trituration with methanol–acetone, was collected by filtration to yield *N*-acetyl-22,27-imino-17β-jerva-5,12-diene-3β,11α,23β-triol (**25**, 130 mg), mp 223—233 °C. This was recrystallized twice from the same solvent for analysis; mp 248—251 °C; $[\alpha]_D$ −22.8° (MeOH); IR, ν_{max} 3320, 1612, 1067, and 1024 cm^{-1}.

Found: C, 73.48; H, 9.50; N, 3.00%. Calcd for $C_{29}H_{45}O_4N$: C, 73.84; H, 9.62; N, 2.97%.

The middle fraction (**26a**, 355 mg), amorphous, showed the following IR and NMR spectrum; ν_{max} ($CHCl_3$) 1724, 1628, 1250, and 1025 cm^{-1} (no OH absorption); τ 9.12 and 8.96 (total 9H?, each d J=6.5 and 5 Hz, 18-, 21- and 26-Me or *vice versa*), 8.73 (3H, s, 19-Me), 7.97 (9H, s, OCOCH_3), and 7.87 (3H, s, NCOCH_3). This was hydrolyzed in the same manner as **25a** and gave amorphous substance, which crystallized on trituration with methanol–acetone and was collected by filtration to yield *N*-acetyl-22,27-imino-12ξ,13ξ,-17β-jerv-5-ene-3β,11β,23β-triol (**26**, 96 mg), mp 217—223 °C. This was recrystallized three times from the same solvent for analysis; mp 241—242 °C; $[\alpha]_D$ −30.2° (MeOH); mass, *m/e* 473 (M^+); IR, ν_{max} 3505, 3395, 1605, 1049, and 1024 cm^{-1}; NMR, τ 9.17, 8.98 and 8.78 (total 9H?, each d J=7, 5 and 6 Hz, 18-, 21- and 26-Me or *vice versa*), 8.76 (3H, s, 19-Me), 7.88 (3H, s, NCOCH_3), and 4.75 (1H, br s W_H=9.5 Hz, H at C_6).

Found: C, 73.27; H, 10.03; N, 2.84%. Calcd for $C_{29}H_{47}O_4N$: C, 73.53; H, 10.00; N, 2.96%.

The least mobile fraction (376 mg), crystalline, was recrystallized from acetone–isopropyl ether to give **24** (=**7a**,

215 mg), mp 213—215 °C; $[\alpha]_D$ −28.3°; mass, *m/e* 555 (M^+), 198 and 156; IR, ν_{max} 3570, 1741, 1635, 1239, and 1023 cm^{-1}; NMR, τ 9.18 and 8.80 (each 3H, d J=6 and 7 Hz, 21- and 26-Me or *vice versa*), 8.74 (3H, s, 19-Me), 8.23 (3H, s, 18-Me), 8.00 (6H, s, $OCOC\underline{H}_3$), 7.89 (3H, s, $NCOC\underline{H}_3$), and 6.58 (1H, br s W_H=5.5 Hz, H at C_{11}).

Found: C, 71.13; H, 8.83; N, 2.57%. Calcd for $C_{33}H_{49}O_6N$: C, 71.32; H, 8.89; N, 2.52%.

Oxidation of 24 (=7a) with chromic anhydride and pyridine. A solution of **24** (=**7a**, 26 mg) in pyridine (1 ml) was treated with chromic anhydride (96 mg) at room temperature overnight under stirring, and then shaken with water and chloroform. The chloroform solution was washed with 1M hydrochloric acid, a 5% sodium bicarbonate solution and water, dried and evaporated to leave oily residue, which showed a single spot but was further purified by preparative tlc (ether–benzene 4: 1, and 1 plate). The main fraction afforded crystalline material (22 mg), which was again dissolved in chloroform. The solution was worked up as usual and the product was recrystallized from acetone–isopropyl ether to give **23** (15 mg), mp 215.5—217 °C, which was identical with an authentic sample.[16,18]

Birch reduction of 24 (=7a). a) To a solution of **24** (=**7a**, 200 mg) in ethylamine (35 ml) was added finely divided lithium (250 mg), and the mixture was stirred vigorously under reflux for 1 hr. The reaction mixture on addition of ammonium chloride became colorless and was worked up in the same manner as for **4**, giving amorphous residue (198 mg), showing only 2 spots. This was acetylated with acetic anhydride (3 ml) and pyridine (3 ml) at room temperature for 28 hr. The product showed 4 spots and was separated into 4 parts by preparative tlc (ether–benzene 1: 2, and 9 plates). The first, mobile fraction (22 mg), amorphous, was not further examined but apparently differed from **6a**, judging from the R_f value. The second, main fraction (149 mg), crystalline, was recrystallized from aqueous methanol to give **2a** (89 mg), mp 191—194 °C, which was identical with the sample obtained from **4**. The third fraction (21 mg), amorphous, was a mixture of two compounds and not further examined. The last, least mobile fraction (48 mg), amorphous, crystallized on trituration with acetone–isopropyl ether to give the starting material **24** (28 mg), mp 208—212 °C.

b) A solution of **24** (=**7a**, 207 mg) in liquid ammonia (50 ml), dry dioxane (20 ml) and dry THF (20 ml) was stirred vigorously with lithium (130 mg) under reflux for 1 hr. After dropwise addition of ethanol (10 ml), the mixture was worked up as usual and gave amorphous substance. Since this contained a considerable amount of the unreacted material **24**, the reduction was again carried out under the same conditions as mentioned above. The resulting amorphous product (185 mg) showed 3 spots and was separated into 2 main fractions by preparative tlc (ether–methanol 9: 1, and 9 plates). The more mobile fraction crystallized on trituration with methanol–acetone and was collected by filtration. The crystalline material (18 mg), mp 220—222 °C, proved to be identical with **6**. The less mobile fraction apparently consisted of deacetylated derivatives of **2a** and **24**, but was not further examined.

Wolff-Kishner Reduction of 23. A solution of diethylene glycol (20 ml) with dissolving sodium (620 mg) was heated to reflux with anhydrous hydrazine (4 ml) and cooled. Compound **23** (400 mg) was added to the solution, whcih was refluxed for 14.5 hr. The condenser was replaced by a distillation apparatus, and the whole solution was heated for 4.5 hr, 2.3 ml of hydrazine being removed. The resulting pale-yellow solution was poured into ice-water (200 ml) and allowed to stand overnight, when precipitates separated out, were collected by filtration, washed with water and dried (320 mg). On the other hand, the aqueous solution obtained on filtration and water washings were combined and extracted with chloroform. The chloroform solution gave amorphous residue (35 mg), which was combined with the afore-mentioned precipitates and acetylated with acetic anhydride (5 ml) and pyridine (5 ml) at room temperature for 17 hr. The product, showing 2 spots, was separated by preparative tlc (ether–benzene 3: 5, and 25 plates). The more mobile fraction (161 mg), amorphous, showed the same IR spectrum and R_f value on tlc as **6a**, and crystallized on trituration with isopropyl ether to give **6a** (69 mg), mp 173—174 °C, which was identical with the sample described already. The less mobile fraction (107 mg), amorphous, was crystallized from aqueous methanol to yield **2a** (71 mg), mp 193—194 °C, identical with the authentic sample.

Hydrogenation of 6a. A solution of **6a** (91 mg) in acetic acid (6 ml) was hydrogenated over prereduced rhodium-platinum (3: 1) catalyst (104 mg)[11] in acetic acid (5 ml) at room temperature for 1.2 hr, when 2.3 mol of hydrogen had been absorbed. The mixture was worked up as usual and gave amorphous residue (113 mg). This was refluxed with 5% potassium hydroxide in methanol (15 ml) for 1.1 hr under nitrogen and afforded amorphous residue (93 mg), which showed 2 spots and was subjected to separation by preparative tlc (ether, and 6 plates). The more mobile fraction (7 mg), amorphous, was not further examined. The less mobile fraction (76 mg) crystallized on trituration with ethyl acetate, mp 180—182 °C, 55 mg. This compound was identical with **14a**.

Hydrolysis of 24 (=7a). A solution of diethylene glycol (5 ml) with dissolving sodium (180 mg) was refluxed with anhydrous hydrazine (1 ml) for 10 min and cooled. After addition of **24** (99 mg), the whole solution was refluxed for 17 hr, cooled and poured onto crushed ice (30 g), when precipitates separated out, were collected by filtration, washed with water and dissolved in methanol. The methanol solution was concentrated to give oily substance, which crystallized on addition of acetone, mp 232—233 °C, 46 mg. This compound was identical with **7** isolated from the Birch reduction products of **4**. This was recrystallized from acetone for analysis; mp 233—235 °C; $[\alpha]_D$ −65.4° (MeOH); mass, *m/e* 429 (M^+), 141 and 114; IR, ν_{max} 3420 and 1046 cm^{-1}.

Found: C, 75.19; H, 10.08; N, 3.19%. Calcd for $C_{27}H_{43}O_3N$: C, 75.48; H, 10.09; N, 3.26%.

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