

Transformation of *D*:*A*-Friedo-18 β -lup-19-en-3-one into *D*:*B*-Friedo-18 β ,19 α *H*-lup-5-en-3 β -ol and a Comment on the Structure of Guimarenol¹⁾

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D:*A*-Friedo-18 β -lup-19-en-3-one was transformed into *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol by two routes, 1) bromination-dehydrobromination of an enol benzoate of *D*:*A*-friedo-18 β ,19 α *H*-lup-3-one and 2) BF₃·Et₂O-catalyzed backbone rearrangement of 3 β ,4 β -epoxy-*D*:*A*-friedo-18 β ,19 α *H*-lupane. The 18 β *H*,19 α *H*-configuration in these *D*:*A*- and *D*:*B*-friedo-type lupane derivatives was determined by means of X-ray diffraction for a 3 α ,4 α -epoxide derived from *D*:*A*-friedo-18 β ,19 α *H*-lup-3 β -ol. The synthetic *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol was found to be not identical with guimarenol isolated from *Ceropegia dichotoma*.

From the viewpoint of acid-catalyzed backbone rearrangement of triterpenes, we are interested in the structure of guimarenol (**1**), a triterpene alcohol obtained from *Ceropegia dichotoma* by González *et al.*²⁾ They proposed a novel *D*:*B*-friedolupane framework with a double bond between C₍₅₎ and C₍₆₎ and a 3 β -hydroxyl group for guimarenol (**1**), though the stereochemistry at C₍₁₃₎, C₍₁₄₎, C₍₁₇₎, C₍₁₈₎, and C₍₁₉₎ remained undetermined.

Only a few reports have been given on investigations on the migrated lupane derivatives, such as isolation of guimarenol (**1**) and lup-18-en-3 β -ol (**2**)²⁾ and preparation of 3 β -acetoxylup-13(18)-ene (**3**) from lupenyl acetate (**4**).³⁾ The synthesis of *D*:*A*-friedo-18 β -lup-19-ene (**5**) and its 3-oxo derivative (**6**) from friedelin (**7**) and also the conversion of **5** into a migrated baccharane derivative, methyl trinorshionanoate (**8**) were recently reported.⁴⁾

Biosynthesis of lupeol (**9**) is presumed to proceed *via* a pentacyclic intermediate (**A**) carrying a positive charge on C₍₂₀₎ or its equivalent species.⁵⁾ Deprotonation of a proton on C₍₂₉₎ would afford lupeol (**9**), while a sequential shift of methyl groups and hydrides followed by removal of a proton on C₍₆₎ would give *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol (**10**) as shown in Fig. 1. Thus, the 18 β *H*- and 19 α *H*-configuration could be biogenetically assumed for migrated lupane derivatives including guimarenol (**1**). This paper describes the synthesis of *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol (**10**) from *D*:*A*-friedo-18 β -lup-19-en-3-one (**6**)^{4b)} and determination of the configuration at C₍₁₈₎ and C₍₁₉₎ of 3 α ,4 α -epoxy-*D*:*A*-friedo-18 β ,19 α *H*-lupane (**11**) derived from a

synthetic intermediate by means of X-ray crystallography. Discrepancy of physical constants and spectral data between the synthetic triterpene (**10**) and guimarenol (**1**) is also described.

The synthesis starts from the conversion of *D*:*A*-friedo-18 β -lup-19-en-3-one (**6**) into an acetate (**13**) *via* an alcohol (**12**). The next step, hydrogenation of the acetate (**13**) seems crucial, since the hydrogenation is likely to occur from both α - and β -sides. However, it was inferred by use of a Dreiding model that hydrogenation from the α -side to generate a 19 β -isopropyl group would take place more easily than that from the β -side. The acetate (**13**) in acetic acid was hydrogenated under atmospheric pressure over platinum catalyst at 40 °C. Although the product (**14**), C₃₂H₅₄O₂ (determined by elemental analysis and mass spectrometry), was found

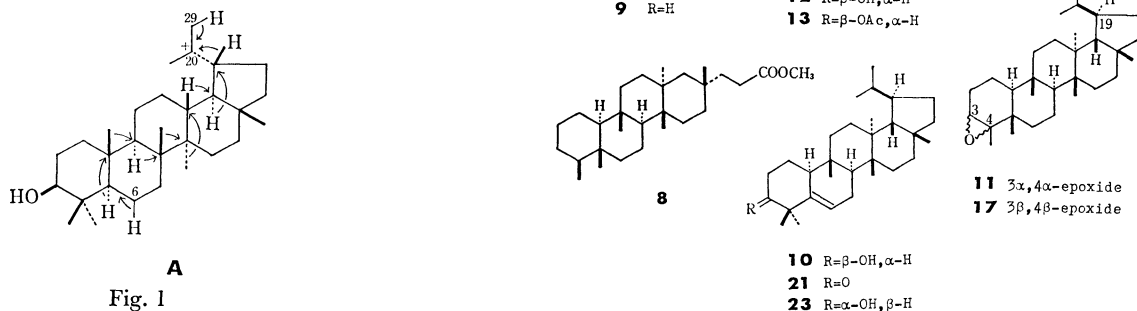
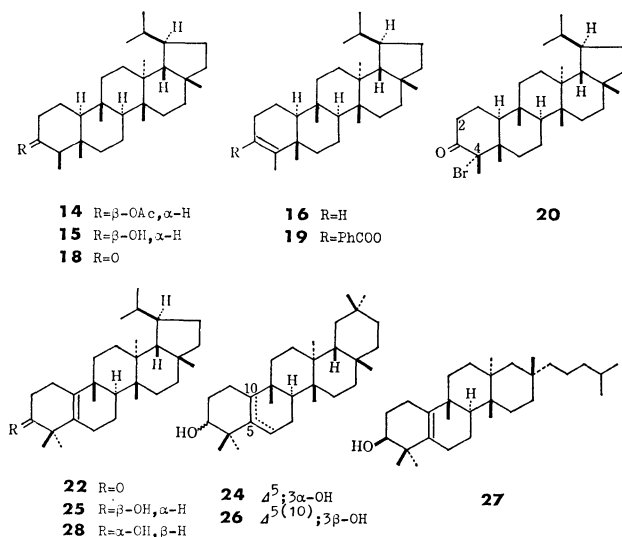


Fig. 1



to be single by GLC and ^1H NMR measurement, the configuration of the 19β-isopropyl group could not be fully established until X-ray analysis clarified that 3α,4α-epoxy-*D*:*A*-friedo-18β,19α*H*-lupane (**11**) derived from the hydrogenation product possesses the desired

19α*H*-configuration (*vide infra*).

Saturated acetate (**14**) was treated with lithium aluminium hydride to give *D*:*A*-friedo-18β,19α*H*-lupane-3β-ol (**15**), which on treatment with phosphoryl chloride in pyridine under reflux, gave *D*:*A*-friedo-18β,19α*H*-lup-3-ene (**16**), $\text{C}_{30}\text{H}_{50}$, showing ^1H NMR signals at δ 5.18 (1H, m, $W_{1/2}=9$ Hz). The dehydration product (**16**) was treated with *m*-chloroperbenzoic acid in chloroform to afford a mixture of two epoxides in a 9:5 ratio, their configurations being easily assigned by ^1H NMR measurement.⁶⁾ The major epoxide with a signal at δ 2.85 (t, $J=2.5$ Hz) was 3α,4α-epoxide (**11**) and the minor one with a signal at δ 2.90 (t, $J=1$ Hz) 3β,4β-epoxide (**17**).

The stereochemistry of the isopropyl group of **14** was unambiguously determined by X-ray diffraction analysis of 3α,4α-epoxy-*D*:*A*-friedo-18β,19α*H*-lupane (**11**). A single crystal of **11** belongs to the monoclinic space group $P2_1$ with cell parameters $a=13.996(6)$, $b=11.461(5)$, $c=8.199(4)$ Å, $\beta=106.34(6)^\circ$ the two molecules being contained in the cell. The intensity data were collected on a Philips PW1100 automatic diffractometer using graphite-monochromated Cu $K\alpha$ radiation. A total of 2494, non-zero, independent reflections with $2\theta \leq 156^\circ$ were measured by means of θ - 2θ scanning.

TABLE 1. ATOMIC POSITIONAL PARAMETERS ($\times 10^4$) AND ANISOTROPIC TEMPERATURE FACTORS^{a)} ($\times 10^4$) WITH ESTIMATED STANDARD DEVIATIONS IN PARENTHESES

Atom	<i>x</i>	<i>y</i>	<i>z</i>	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C (1)	3418(6)	5633(0)	9079(9)	67(5)	94(7)	147(13)	16(5)	30(7)	29(9)
C (2)	4167(6)	4633(9)	9790(11)	53(5)	113(9)	245(18)	5(6)	31(8)	57(11)
C (3)	4917(6)	4420(8)	8815(11)	58(5)	81(7)	217(17)	5(5)	17(7)	4(9)
C (4)	4946(5)	5074(7)	7301(10)	50(4)	70(6)	194(14)	4(4)	24(6)	-11(8)
C (5)	4204(5)	6078(7)	6693(9)	51(4)	70(6)	161(12)	0(4)	28(6)	-9(8)
C (6)	3997(5)	6202(8)	4732(9)	49(4)	113(8)	171(13)	1(5)	42(6)	18(9)
C (7)	3126(5)	7077(8)	3985(10)	57(4)	96(8)	189(14)	-5(5)	49(7)	32(9)
C (8)	2176(5)	6565(6)	4345(8)	45(4)	58(5)	119(10)	1(4)	39(5)	10(6)
C (9)	2304(5)	6566(6)	6298(8)	48(4)	46(5)	136(11)	-2(4)	35(5)	-5(6)
C (10)	3218(5)	5777(6)	7113(8)	50(4)	56(5)	139(11)	-4(4)	35(5)	1(7)
C (11)	1355(5)	5980(6)	6591(8)	46(4)	68(6)	111(10)	3(4)	33(5)	22(6)
C (12)	367(5)	6491(7)	5442(7)	48(4)	77(6)	93(10)	7(4)	30(5)	10(7)
C (13)	276(5)	6395(6)	3533(7)	50(4)	45(5)	105(10)	4(3)	37(5)	5(6)
C (14)	1179(5)	7093(6)	3180(8)	52(4)	51(5)	117(10)	4(4)	42(5)	11(6)
C (15)	1129(5)	6880(7)	1277(8)	61(4)	100(8)	97(10)	10(5)	42(6)	13(8)
C (16)	162(6)	7385(8)	69(10)	69(5)	115(9)	116(11)	14(6)	52(6)	38(8)
C (17)	-827(5)	7143(6)	514(8)	63(4)	64(6)	116(11)	6(5)	39(6)	10(7)
C (18)	-726(5)	6963(6)	2481(7)	50(4)	51(5)	95(10)	4(4)	33(5)	7(6)
C (19)	-1669(5)	6249(6)	2514(8)	51(4)	65(6)	126(11)	-2(4)	32(5)	10(7)
C (20)	-2494(5)	6945(7)	3021(10)	55(4)	77(7)	179(13)	3(5)	36(6)	13(8)
C (21)	-2080(6)	5688(8)	709(9)	77(5)	92(7)	137(12)	-21(6)	29(7)	-17(8)
C (22)	-1328(6)	6016(8)	-321(9)	89(6)	82(7)	122(12)	-10(6)	39(7)	-17(8)
C (23)	5924(6)	5112(9)	6755(12)	58(5)	124(10)	259(19)	20(6)	58(8)	-9(12)
C (24)	4739(6)	7208(8)	7601(12)	71(5)	69(7)	277(19)	-15(5)	34(8)	-20(10)
C (25)	2381(6)	7803(7)	7141(10)	68(5)	61(6)	191(14)	8(5)	35(7)	-32(8)
C (26)	1095(6)	8408(6)	3431(10)	75(5)	42(5)	183(14)	0(4)	47(7)	9(7)
C (27)	303(5)	5082(6)	3088(9)	63(4)	42(5)	181(13)	9(4)	45(6)	3(7)
C (28)	-1517(6)	8190(7)	-138(10)	77(5)	83(7)	153(13)	26(5)	43(7)	48(8)
C (29)	-2130(6)	7383(8)	4868(10)	71(5)	116(9)	167(14)	18(6)	57(7)	-14(10)
C (30)	-3423(6)	6185(10)	2848(13)	65(5)	137(11)	322(22)	-22(7)	72(9)	-20(14)
O	4518(4)	3926(5)	7117(7)	64(3)	61(4)	258(12)	7(3)	17(5)	-18(6)

a) The form of the anisotropic temperature factor is: $T = \exp(-B_{11}h^2 - B_{22}k^2 - B_{33}l^2 - 2B_{12}hk - 2B_{13}hl - 2B_{23}kl)$.

4 Hz) with those of *D*:*B*-friedoolean-5(10)-en-3 β -ol (**26**)^{6b}) (δ 3.45, 1H, dd; $J=9.5$ and 4.5 Hz) and *D*:*B*-friedobacchar-5(10)-en-3 β -ol (**27**)^{6a}) (δ 3.48, 1H, dd; $J=10$ and 4 Hz).

The other fraction with a larger R_f value on TLC separation was found to be a 2:1 mixture of two alcohols by HPLC examination and was separated by preparative HPLC into two alcohols **28** ($R_t=22.8$ min) and **10** ($R_t=20.3$ min). The major alcohol (**28**) was found to be *D*:*B*-friedo-18 β ,19 α *H*-lup-5(10)-en-3 α -ol from the ¹H NMR spectrum and chemical conversion. The two alcohols **25** and **28** gave the same original ketone (**22**) on oxidation with chromium trioxide-pyridine complex. The fourth alcohol (**10**) should be the desired *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol. However, yield was less than 3% from the bromide (**20**). No satisfactory characterization could be achieved.

Treatment of 3 β ,4 β -epoxides of *D*:*A*-friedo-type triterpenes with boron trifluoride etherate gives a mixture of backbone-rearranged products, from which *D*:*B*-friedo-*A*⁵- and -*A*⁵⁽¹⁰⁾-triterpene 3 β -alcohols are obtained. For example, *D*:*B*-friedobacchar-5-en-3 β -ol was obtained from 3 β ,4 β -epoxyshionane¹³) and *D*:*B*-friedoolean-5-en-3 β -ol from 3 β ,4 β -epoxyfriedelane^{6b}) together with their 5(10)-ene isomers, respectively. 3 β ,4 β -Epoxy-*D*:*A*-friedo-18 β ,19 α *H*-lupane (**17**) was treated with boron trifluoride etherate in benzene to give a complex mixture, from which an alcohol was obtained. The ¹H NMR spectrum of the alcohol showed the presence of an olefinic proton [at δ 5.65 (1H, m, $W_{1/2}=7$ Hz)] and a proton attached to a hydroxyl-bearing carbon atom [at δ 3.45 (1H, m, $W_{1/2}=7$ Hz)].^{6b}) The structure, *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol was established for this alcohol (**10**) by the following evidence. **10** was oxidized with chromium trioxide-pyridine complex to give a ketone, *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3-one (**21**), identical with that obtained by the oxidation of *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 α -ol (**23**). Retention times on GLC and HPLC examinations and R_f value on TLC of **10** were identical with those of the fourth alcohol obtained by the bromination-dehydrobromination reaction of the ketone (**18**)

(*vide supra*).

The ¹H NMR, mass spectral data, and melting points of the four alcohols (**10**, **23**, **25**, and **28**) and the ketones (**21** and **22**) together with those of guimarenol (**1**) and guimarenone (**29**) are given in Table 2. The physical and spectral data of guimarenol (**1**) and the corresponding ketone, guimarenone (**29**), differ distinctly from those of the synthetic *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol (**10**) and the corresponding 3-one (**21**), respectively. The structure of guimarenol (**1**)²) should be reinvestigated.

Experimental

General Procedure. Melting points were measured on a Mel-temp capillary melting point apparatus (Laboratory Devices) and are uncorrected. IR spectra were measured in Nujol mull with a Hitachi-EPI-G2 spectrometer or a Hitachi 260-30 spectrometer, mass spectra on a Hitachi RMU-6-Tokugata mass spectrometer at 70 eV with a direct inlet system, and high resolution mass spectra on a JMS-D300 (JEOL) mass spectrometer. Relative intensities are given in parentheses. ¹H NMR spectra were measured with a Hitachi R-20B (60 MHz) spectrometer, a Varian EM-390 (90 MHz) spectrometer or a JNM-FX60 FT-NMR (60 MHz) spectrometer (JEOL). Chemical shifts are given in δ downfield from TMS as an internal standard and coupling constants in Hz. GLC analyses were carried out with a Shimadzu Gas Chromatograph GC-6A equipped with a hydrogen flame ionization detector (column: Dexsil 300GC, temperature 270–290 °C). HPLC analysis and preparation were carried out on a Waters Liquid Chromatograph ALC/GPS 202/401 at room temperature with an RI detector (column: μ -Porasil 1/4 (inch) $\times$ 1 (foot); solvent system: 1.5% diethyl ether-hexane (unless otherwise described); flow rate: 3 ml/min (unless otherwise described); pressure: ca. 700 psi). TLC was carried out on Kieselgel 60 GF₂₅₄ (E. Merck) coated in 0.25 mm thickness (for analytical) and in 0.5 mm thickness (for preparative). Wakogel C-200 (Wako) was used for column chromatography.

D:*A*-Friedo-18 β -lup-19-en-3 β -yl Acetate (**13**). Excess of sodium borohydride (ca. 10 mg) was added to a solution of *D*:*A*-friedo-18 β -lup-19-en-3-one (**6**; 7.5 mg) in methanol (30 ml) at room temperature, the mixture being stirred

TABLE 2.

Compound	Mp (°C)	¹ H NMR	MS
Guimarenol (1)	276–278	δ 5.60 (1H, m) δ 3.55 (1H, t, $W_{1/2}=6$ Hz)	426 (M ⁺ ; 8%) 274 (100%)
5-en-3 β -ol (10)	166–167	δ 5.65 (1H, m) δ 3.45 (1H, m, $W_{1/2}=7$ Hz)	426 (M ⁺ ; 7%) 274 (100%)
5-en-3 α -ol (23)	181–182	δ 5.61 (1H, m, $W_{1/2}=9$ Hz) δ 3.20 (1H, dd, $J=10$, $J=4$ Hz)	426 (M ⁺ ; 10%) 274 (100%)
5(10)-en-3 β -ol (26)	191–193	δ 3.48 (1H, dd, $J=10$, $J=4$ Hz)	426 (M ⁺ ; 13%) 408 (100%) 205 (72%)
5(10)-en-3 α -ol (28)	195.5–196	δ 3.48 (1H, dd, $J=10$, $J=4$ Hz)	426 (M ⁺ ; 10%) 205 (100%)
Guimarenone (29)	196–200	δ 5.75 (1H, m)	424 (M ⁺ ; 26%) 274 (100%)
5-en-3-one (21)	149–153	δ 5.63 (1H, m)	424 (M ⁺ ; 11%) 274 (100%)
5(10)-en-3-one (22)	180–182		424 (M ⁺ ; 68%) 205 (100%)

overnight. The usual work-up and purification by preparative TLC (benzene: diethyl ether=9 : 1) gave D : A-friedo-18 β -lup-19-en-3 β -ol (**12**; 7.2 mg) in 95% yield; mp 173—175 °C (crystallized from acetone); IR 3460 cm⁻¹; ¹H NMR (CDCl₃) δ 0.8—1.0 (18H, 6 $\times$ CH₃), 1.65 (6H, br s; >C=C(CH₃)₂), and 3.75 (1H, m, $W_{1/2}$ =6 Hz); MS m/e 426 (M⁺; 17) and 275 (100).

19-En-3 β -ol (**12**; 7.2 mg) dissolved in pyridine (1 ml) was treated with acetic anhydride (1 ml) at room temperature and the mixture was left overnight. The usual work-up and purification by preparative TLC (benzene) gave D : A-friedo-18 β -lup-19-en-3 β -yl acetate (**13**; 6.8 mg) in 86% yield; mp 240—242.5 °C (crystallized from acetone); IR 1738 cm⁻¹; ¹H NMR (CDCl₃) δ 0.75—0.95 (18H, 6 $\times$ CH₃), 1.63, 1.67 (each 3H, br s; >C=C(CH₃)₂), 2.04 (3H, s), and 4.92 (1H, m, $W_{1/2}$ =7 Hz); MS m/e 468 (M⁺; 60) and 317 (100); Found: C, 81.74; H, 11.09%. Calcd for C₃₂H₅₂O₂: C, 81.99; H, 11.18%.

D : A-Friedo-18 β ,19 α H-lup-3 β -yl Acetate (**14**). The acetate (**13**; 632.2 mg) in acetic acid (350 ml) was hydrogenated in the presence of catalyst [prepared from platinum dioxide (851 mg)] under atmospheric pressure at 40 °C for 3.5 d. The catalyst was filtered off, and the solvent distilled off. The residue was purified by silica gel (35 g) column chromatography to give quantitatively a dihydro derivative, D : A-friedo-18 β ,19 α H-lup-3 β -yl acetate (**14**; 637 mg); mp 251—253 °C (crystallized from acetone); IR 1735 cm⁻¹; ¹H NMR (CDCl₃) δ 0.8—1.0 (18H, 6 $\times$ CH₃), 2.03 (6H, s), and 4.94 (1H, m, $W_{1/2}$ =6 Hz); MS m/e 470 (M⁺; 58) and 410 (100); Found: C, 81.70; H, 11.81%. Calcd for C₃₂H₅₄O₂: C, 81.64; H, 11.56%.

D : A-Friedo-18 β ,19 α H-lup-3 β -ol (**15**). The saturated acetate (**14**; 370 mg) dissolved in tetrahydrofuran (200 ml), was treated with lithium aluminium hydride (616 mg) under reflux for 1 h. The usual work-up gave D : A-friedo-18 β ,19 α H-lup-3 β -ol (**15**; 327 mg) in 97% yield; mp 225—227 °C (crystallized from acetone); IR 3440 cm⁻¹; ¹H NMR (CDCl₃) δ 0.8—1.1 (24H, 8 $\times$ CH₃) and 3.75 (1H, m, $W_{1/2}$ =7 Hz); MS m/e 428 (M⁺; 100).

D : A-Friedo-18 β ,19 α H-lup-3-ene (**16**). Freshly distilled phosphoryl chloride (1.8 ml) was added to a solution of 3 β -ol (**15**; 317.3 mg) in dry pyridine (60 ml), the mixture being refluxed for 40 min. The residue obtained by the usual work-up was chromatographed on silica gel (60 g) impregnated with 25% silver nitrate to give D : A-friedo-18 β ,19 α H-lup-3-ene (**16**; 254 mg) in 84% yield; mp 169—170 °C (crystallized from acetone); IR 795 cm⁻¹; ¹H NMR (CDCl₃) δ 0.95—1.15 (21H, 7 $\times$ CH₃), 1.56 (3H, d; J =1.5 Hz), and 5.18 (1H, m, $W_{1/2}$ =9 Hz); MS m/e 410 (M⁺; 65) and 318 (100); Found: C, 87.78; H, 12.34%. Calcd for C₃₀H₅₀: C, 87.73; H, 12.27%.

Epoxidation of D : A-Friedo-18 β ,19 α H-lup-3-ene (**16**). *m*-Chloroperbenzoic acid (578 mg) was added to a solution of the 3-ene (**16**; 254 mg) in chloroform (150 ml) at 0 °C, the solution being stirred at the same temperature for 1.5 h. A saturated aqueous sodium thiosulfate (50 ml) and a saturated aqueous sodium hydrogencarbonate (30 ml) were added to the solution, the mixture being stirred for 30 min at room temperature. Extraction with chloroform and the usual work-up gave a residue which was purified by preparative TLC [Kieselgel G (E. Merck); hexane: chloroform=3 : 2] to give 3 α ,4 α -epoxy-D : A-friedo-18 β ,19 α H-lupane (**11**; 157.5 mg) and 3 β ,4 β -epoxy-D : A-friedo-18 β ,19 α H-lupane (**17**; 87.5 mg) in 60 and 33% yields, respectively. 3 α ,4 α -Epoxy-D : A-friedo-18 β ,19 α H-lupane (**11**): mp 200—202 °C (crystallized from acetone); ¹H NMR (CDCl₃) δ 0.85 (15H, 5 $\times$ CH₃), 0.96, 1.07, 1.19 (each 3H, s) and 2.85 (1H, t; J =2.5 Hz); MS m/e 426 (M⁺; 77) and 411 (100); Found: C, 84.72; H, 11.95%. Calcd for

C₃₀H₅₀O: C, 84.44; H, 11.81%. 3 β ,4 β -Epoxy-D : A-friedo-18 β ,19 α H-lupane (**17**): mp 215—216 °C crystallized from acetone; ¹H NMR (CDCl₃) δ 0.88 (15H, 5 $\times$ CH₃), 0.96, 1.05, 1.17 (each 3H, s) and 2.90 (1H, t; J =1 Hz); MS m/e 426 (M⁺; 100); Found: C, 84.67; H, 11.94%. Calcd for C₃₀H₅₀O: C, 84.44; H, 11.81%.

D : A-Friedo-18 β ,19 α H-lup-3-one (**18**). The 3 β -ol (**15**; 246 mg) dissolved in acetone (150 ml) was treated with the Jones reagent at 0 °C for 1 h. The usual work-up gave D : A-friedo-18 β ,19 α H-lup-3-one (**18**; 236 mg) in 96% yield; mp 260—262 °C (crystallized from acetone); IR 1715 cm⁻¹; ¹H NMR (CDCl₃) δ 0.72 (3H, s) and 0.8—1.0 (21H, 7 $\times$ CH₃); ¹H NMR (CDCl₃) using Eu(fod)₃-d₂₇/18=0.2 (M/M) δ 1.72 (3H, d; J =7 Hz; 4 β -CH₃); MS m/e 426 (M⁺; 100); Found: C, 84.66; H, 11.79%. Calcd for C₃₀H₅₀O: C, 84.44; H, 11.81%.

3-Benzoyloxy-D : A-friedo-18 β ,19 α H-lup-3-ene (**19**). D : A-friedo-18 β ,19 α H-lup-3-one (**18**; 144 mg) was treated with benzoyl chloride (2 ml) under reflux for 2 h. The solution was cooled to 0 °C, methanol (ca. 5 ml) being added in order to destroy excess benzoyl chloride. When the mixture was allowed to stand for 30 min, crystals began to precipitate. The precipitate was collected on a filter paper and washed with methanol. 3-Benzoyloxy-D : A-friedo-18 β ,19 α H-lup-3-ene (**19**; 168 mg) was obtained in 94% yield; mp 255—256 °C (crystallized from acetone); IR 1732 cm⁻¹; ¹H NMR (CDCl₃) δ 0.9—1.0 (18H, 6 $\times$ CH₃), 1.09, 1.49 (each 3H, s), 7.4—7.7 (3H, m), and 8.0—8.3 (2H, m); MS m/e 530 (M⁺; 5) and 105 (100); Found: C, 83.75; H, 10.13%. Calcd for C₃₇H₅₄O₂: C, 83.72; H, 10.25%.

4 α -Bromo-D : A-friedo-18 β ,19 α H-lup-3-one (**20**). A mixture of bromine (0.1 ml) and pyridine (0.5 ml) was added to a chloroform solution (5 ml) of the enol benzoate (**19**; 50.3 mg) at room temperature. After being stirred for 3 h, a small amount of aqueous sodium thiosulfate was added and the mixture was stirred for several hours. The usual work-up and purification by preparative TLC (hexane: benzene=1 : 1) gave 4 α -bromo-D : A-friedo-18 β ,19 α H-lup-3-one (**20**; 31.6 mg) in 66% yield; mp 192.5—194.5 °C (crystallized from methanol); IR 1715 cm⁻¹; ¹H NMR (CDCl₃) δ 0.8—1.0 (21H, 7 $\times$ CH₃), 1.71 (3H, s), and 3.38 (1H, ddd; J =20, 13, and 8 Hz); MS m/e 506 (M⁺; 12), 504 (M⁺; 12), and 123 (100); Found: m/e 506.2946. Calcd for C₃₀H₄₉OBr: M, 506.2903. Found: m/e 504.2992. Calcd for C₃₀H₄₉O⁷⁹Br: M, 504.2967.

Dehydrobromination of 4 α -Bromo-D : A-friedo-18 β ,19 α H-lup-3-one (**20**). A mixture of silver acetate (34 mg), water (0.3 ml), and acetic acid (16 ml) was added to an ethereal solution (12 ml) of the 4 α -bromo ketone (**20**; 31.6 mg). The solvent was distilled off until the vapor temperature reached ca. 100 °C, the solution then being refluxed for 1 h. The usual work-up gave a residue (24.6 mg) which was purified by preparative TLC (benzene) to give a ca. 1 : 2 mixture (19.6 mg) of D : B-friedo-18 β ,19 α H-lup-5-en-3-one (**21**) and D : B-friedo-18 β ,19 α H-lup-5(10)-en-3-one (**22**) in 74% yield. The relative ratio of the product was estimated from the peak area of GLC and the integrated area of olefinic proton signal in the ¹H NMR spectrum. These two olefinic isomers, however, could not be separated from each other by TLC or HPLC.

Reduction of the Mixture of Keto Olefins (**21** and **22**). A mixture (19.6 mg) of two olefinic isomers (**21** and **22**) was dissolved in methanol (5 ml) and kept at 0 °C. Excess sodium borohydride (ca. 30 mg) was added and the solution was stirred for 1 h. The usual work-up and purification by preparative TLC (benzene) gave a pair of mixtures. GLC examination showed that a mixture (16.6 mg) with a smaller R_f value on TLC consists of D : B-friedo-18 β ,19 α H-lup-5-en-3 α -ol (**23**) and D : B-friedo-18 β ,19 α H-lup-5(10)-en-3 β -ol (**25**), and the other

mixture (2.1 mg) with a larger R_f value consists of *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol (**10**) and *D*:*B*-friedo-18 β ,19 α *H*-lup-5(10)-en-3 α -ol (**28**). The former mixture was separated by preparative HPLC into *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 α -ol (**23**; 5.2 mg) and *D*:*B*-friedo-18 β ,19 α *H*-lup-5(10)-en-3 β -ol (**25**; 9.8 mg). *D*:*B*-Friedo-18 β ,19 α *H*-lup-5-en-3 α -ol (**23**): mp 181–182 °C (crystallized from acetone); IR 3320 and 825 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.8–1.0 (24H, $8 \times \text{CH}_3$), 3.20 (1H, dd, $J=10$ and 4 Hz), and 5.61 (1H, m, $W_{1/2}=9$ Hz); MS m/e 426 (M^+ ; 10) and 274 (100); HPLC (solvent system: 10% diethyl ether–hexane; flow rate: 2 ml/min) $R_t=38.9$ min; Found: m/e 426.3808. Calcd for $\text{C}_{30}\text{H}_{50}\text{O}$: M, 426.3860. *D*:*B*-Friedo-18 β ,19 α *H*-lup-5(10)-en-3 β -ol (**25**): mp 191–193 °C (crystallized from acetone); IR 3350 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.8–1.05 (24H, $8 \times \text{CH}_3$) and 3.48 (1H, dd, $J=10$ and 4 Hz); MS m/e 426 (M^+ ; 13), 408 (100), and 205 (72); HPLC (solvent system: 10% diethyl ether–hexane; flow rate: 2 ml/min) $R_t=41.3$ min; Found: m/e 426.3846. Calcd for $\text{C}_{30}\text{H}_{50}\text{O}$: M, 426.3860.

The latter mixture of **10** and **28** was separated by preparative HPLC into *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol (**10**; less than 0.5 mg) and -5(10)-en-3 α -ol (**28**; 1.1 mg). *D*:*B*-Friedo-18 β ,19 α *H*-lup-5(10)-en-3 α -ol (**28**): mp 195.5–196 °C (crystallized from acetone); IR 3620 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.90 (6H, d; $J=7$ Hz, $(\text{CH}_3)_2\text{CH}-$), 0.97, 1.03 (each 3H, s), 0.89, 1.00 (each 6H, s, $2 \times \text{CH}_3$), and 3.48 (1H, dd, $J=10$ and 4 Hz); MS m/e 426 (M^+ ; 10) and 205 (100); HPLC (solvent system: 10% diethyl ether–hexane; flow rate: 2 ml/min) $R_t=22.8$ min; Found: m/e 426.3880. Calcd for $\text{C}_{30}\text{H}_{50}\text{O}$: M, 426.3860.

*Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 3 β ,4 β -Epoxy-D:A-friedo-18 β ,19 α *H*-lupane (17) in Benzene.*

A solution of 3 β ,4 β -epoxy-*D*:*A*-friedo-18 β ,19 α *H*-lupane (**17**; 47 mg) in benzene (25 ml) was treated with boron trifluoride etherate (0.3 ml) at room temperature for 1 h. The usual work-up gave a mixture, which was separated by preparative TLC (benzene) into *D*:*A*-friedo-18 β ,19 α *H*-lupane-3-one (**18** 0.5 mg), *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol (**10**; 4.4 mg), and a complex mixture of alcohols (37.2 mg). *D*:*B*-Friedo-18 β ,19 α *H*-lup-5-en-3 β -ol (**10**): mp 166–167 °C (crystallized from acetone); IR 3400 (br), 1195, 1045, 973, and 825 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.88, 1.03, 1.13, 1.24 (each 3H, s; $t\text{-CH}_3$), 0.90 (6H, d; $J=6$ Hz; $(\text{CH}_3)_2\text{CH}-$), 0.97 (6H, s, $2 \times t\text{-CH}_3$), 3.45 (1H, m, $W_{1/2}=7$ Hz), and 5.65 (1H, m, $W_{1/2}=7$ Hz); MS m/e 426 (M^+ ; 7) and 274 (100); HPLC (solvent system: 10% diethyl ether–hexane; flow rate: 2 ml/min) $R_t=20.3$ min; Found: m/e 426.3852. Calcd for $\text{C}_{30}\text{H}_{50}\text{O}$: M, 426.3860.

D:*B*-Friedo-18 β ,19 α *H*-lup-5-en-3-one (**21**). a): A large excess of chromium trioxide–pyridine complex in pyridine (0.5 ml) was added to a solution of *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 α -ol (**23**; 4.3 mg) in dichloromethane (3 ml), the solution being stirred at room temperature for 6 h. The usual work-up and preparative TLC (benzene) gave *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3-one (**21**; 1.6 mg).

b): The same oxidation of *D*:*B*-friedo-18 β ,19 α *H*-lup-5-en-3 β -ol (**10**; 4.4 mg) in dichloromethane (3 ml) with a large excess of chromium trioxide–pyridine complex in pyridine (0.5 ml) gave **21** (1.6 mg); mp 149–153 °C (crystallized from acetone); IR 1718 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.82–0.90 (each 3H, s), 0.83 (6H, d; $J=7$ Hz; $(\text{CH}_3)_2\text{CH}-$), 1.21 (12H, s, $4 \times \text{CH}_3$), and 5.63 (1H, m, $W_{1/2}=11$ Hz); MS m/e 424 (M^+ ; 11), 274 (100), and 123 (93); Found: m/e 424.3731. Calcd for $\text{C}_{30}\text{H}_{48}\text{O}$: M, 424.3705.

D:*B*-Friedo-18 β ,19 α *H*-lup-5(10)-en-3-one (**22**). a): Pyridinium chlorochromate¹⁴ (16 mg) was added to a solution of *D*:*B*-friedo-18 β ,19 α *H*-lup-5(10)-en-3 α -ol (**28**; 12.5 mg) in dichloromethane (3 ml), the solution being stirred at room

temperature for 5 h. The usual work-up and silica gel chromatography gave *D*:*B*-friedo-18 β ,19 α *H*-lup-5(10)-en-3-one (**22**; 10.1 mg).

b): A solution of *D*:*B*-friedo-18 β ,19 α *H*-lup-5(10)-en-3 β -ol (**25**; 5.2 mg) in dichloromethane (3 ml) was oxidized with pyridinium chlorochromate (41 mg) in the same way as above to give **22** (5 mg); mp 180–182 °C (crystallized from acetone); IR 1715 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.8–0.95 (12H, $4 \times \text{CH}_3$), 0.97, 1.03, 1.13, and 1.16 (each 3H, s); MS m/e 424 (M^+ ; 68) and 205 (100); Found: m/e 424.3705. Calcd for $\text{C}_{30}\text{H}_{48}\text{O}$: M, 424.3705.

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