Transformation of *D* : *A*-Friedo-18β-lup-19-en-3-one into *D* : *B*-Friedo-18β,19α*H*-lup-5-en-3β-ol and a Comment on the Structure of Guimarenol[1)]

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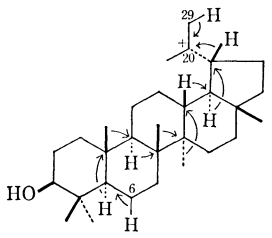
D:*A*-Friedo-18β-lup-19-en-3-one was transformed into *D*:*B*-friedo-18β,19α*H*-lup-5-en-3β-ol by two routes, 1) bromination-dehydrobromination of an enol benzoate of *D*:*A*-friedo-18β,19α*H*-lupan-3-one and 2) $BF_3 \cdot Et_2O$-catalyzed backbone rearrangement of 3β,4β-epoxy-*D*:*A*-friedo-18β,19α*H*-lupane. The 18β*H*,19α*H*-configuration in these *D*:*A*- and *D*:*B*-friedo-type lupane derivatives was determined by means of X-ray diffraction for a 3α,4α-epoxide derived from *D*:*A*-friedo-18β,19α*H*-lupan-3β-ol. The synthetic *D*:*B*-friedo-18β,19α*H*-lup-5-en-3β-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 3β-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-3β-ol (**2**)[2)] and preparation of 3β-acetoxy-19α*H*-lup-13(18)-ene (**3**) from lupenyl acetate (**4**).[3)] The synthesis of *D*: *A*-friedo-18β-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)]

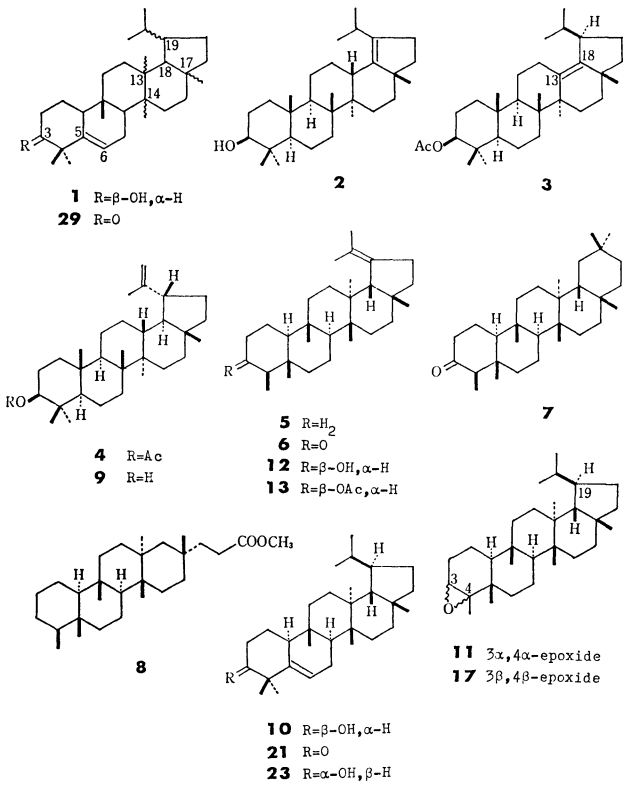
Biosynthesis of lupeol (**9**) is presumed to proceed *via* a pentacyclic intermediate (**A**) carrying a positive charge on $C_{(20)}$ or its equivalent species.[5)] Deprotonation of a proton on $C_{(29)}$ would afford lupeol (**9**), while a sequential shift of methyl groups and hydrides followed by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

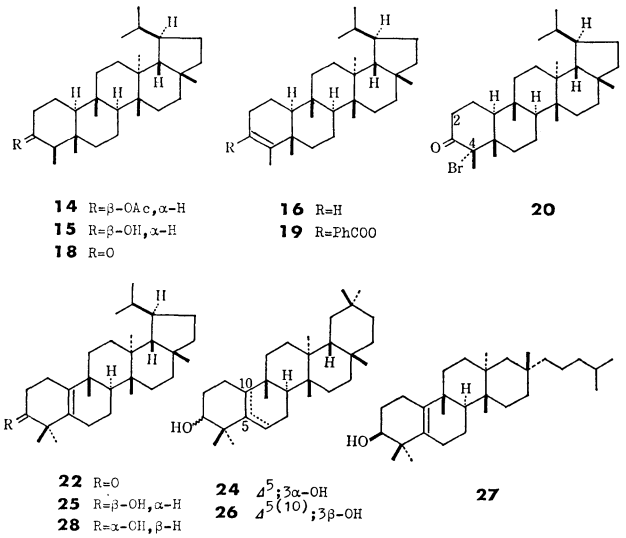


A

Fig. 1

The synthesis starts from the conversion of *D* : *A*-friedo-18β-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 19β-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**), $C_{32}H_{54}O_2$ (determined by elemental analysis and mass spectrometry), was found





to be single by GLC and ^{1}H 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*-lupan-3β-ol (**15**), which on treatment with phosphoryl chloride in pyridine under reflux, gave *D* : *A*-friedo-18β,19α*H*-lup-3-ene (**16**), $C_{30}H_{50}$, showing ^{1}H 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 ^{1}H 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, β=106.34(6)° the two molecules being contained in the cell. The intensity data were collected on a Phlips PW1100 automatic diffractometer using graphite-monochromated Cu $K\alpha$ radiation. A total of 2494, non-zero, independent reflections with $2\theta \leq 156°$ 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	x	y	z	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: $T=\exp(-B_{11}h^2-B_{22}k^2-B_{33}l^2-2B_{12}hk-2B_{13}hl-2B_{23}kl)$.

The intensities were corrected for Lorentz and polarization factors, but not for absorptions. The structure was solved by the direct method using program MULTAN.[7] An E-map calculated from 323 reflections with $|E| \leq 1.5$ revealed the locations of 25 nonhydrogen atoms out of 31, and all the other nonhydrogen atoms emerged in successive Fourier maps. The structural parameters were refined by the block-diagonal least-squares calculations assuming anisotropic thermal vibrations. The final R-factor was 9.9% excluding hydrogen atoms.[8] The weighting scheme $\sqrt{w}=20.0/|F_0|$ when $|F_0| \geq 20.0$, $\sqrt{w}=1.0$ when $20.0>|F_0| \geq 3.0$, and $\sqrt{w}=0.8$ when $|F_0|<3.0$ was applied. The atomic scattering factors were taken from International Tables for X-ray Crystallography.[9] The atomic positional and thermal parameters are given in Table 1. There are no abnormal bond lengths and angles as compared with those found in this type of compound except for the bond lengths $C_{(17)}$–$C_{(18)}$ and $C_{(13)}$–$C_{(14)}$ of 1.592 and 1.589 Å, respectively (Figs. 2a and 2b). The lengthening of the C–C bond at the fully substituted ring juncture is commonly observed in triterpenes, and for the above mentioned two bonds; the effect of repulsions between the 1,3-diaxial substituted groups may be responsible for the lengthening. Figure 3 shows a computer-generated perspective drawing of the molecule of the epoxide (**11**), with the 19αH-configuration as well as the 18βH-configuration.

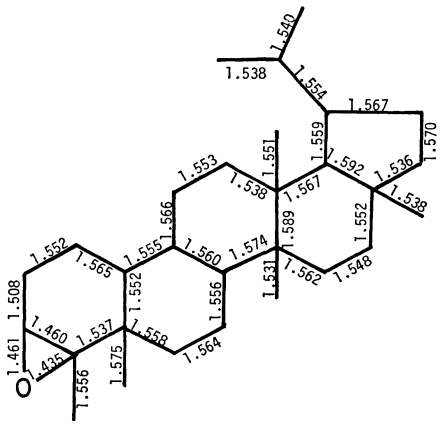


Fig. 2a. Bond lengths (l/Å) of **11**.

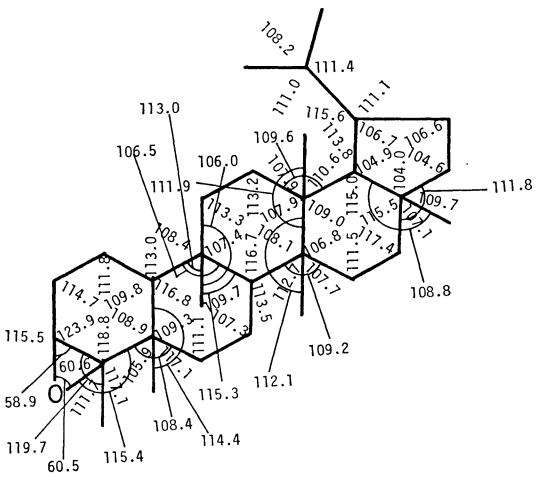


Fig. 2b. Bond angles (Φ/°) of **11**.

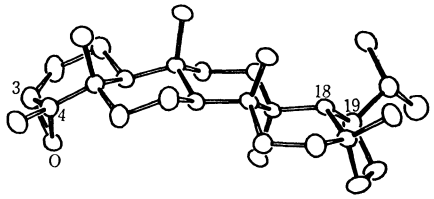


Fig. 3. Perspective view of **11**.

The saturated alcohol (**15**) was subjected to oxidation with the Jones reagent to give a ketone (**18**). The ketone is formulated D : as A-friedo-18β,19αH-lupan-3-one, corresponding biogenetically to the ultimate rearranged product in the migrated lupane series.

The conversion of a D: A-friedo type 3-keto triterpene into a D : B-friedo type ketone was carried out by the bromination-dehydrobromination reaction.[10,11] On treatment with benzoyl chloride under reflux, D : A-friedo-18β,19αH-lupan-3-one (**18**) gave 3-benzoyloxy-D : A-friedo-18β,19αH-lup-3-ene (**19**) selectively in a good yield. The absence of Δ^2-isomer was indicated by ^{1}H NMR measurement. The reaction product, after recrystallization from methanol, was brominated with bromine in pyridine at room temperature[10] to afford a monobromide (**20**), $C_{30}H_{49}OBr$ (M^+ 506.2946 and 504.2992), ^{1}H NMR δ 1.71 (3H, s) and δ 3.38 (1H, ddd; J=20, 13, and 8 Hz). The 4α-orientation of the bromine atom was deduced by the ^{1}H NMR spectrum: the signals at δ 3.38 were assignable to a $C_{(2\alpha)}$–H and the down-field shift was ascribed to a 1,3-diaxial relationship between the $C_{(4\alpha)}$–Br and the $C_{(2\alpha)}$–H.

The 4α-bromo derivative (**20**) was subjected to reaction with silver acetate in a mixture of diethyl ether and acetic acid.[11] The reaction product was purified by preparative TLC to afford a mixture of D : B-friedo-18β,19αH-lup-5-en-3-one (**21**) and -5(10)-en-3-one (**22**). The relative amount of two isomeric ketones (**21** and **22**) was estimated to be about 1 : 2 by GLC examination and ^{1}H NMR measurement. Since the mixture gave only one spot on TLC and only one peak on HPLC examination, separation of the mixture was abandoned.

The mixture was therefore reduced with sodium borohydride to afford a mixture of two pairs of epimeric alcohols. Although the alcohol mixture could not be separated into four components by a single procedure, it could be separated into two fractions by TLC, each fraction being further separated into two components by HPLC. Thus, the mixture was subjected to separation by preparative TLC into two fractions, a major fraction (R_f 0.3) and a minor one (R_f 0.4). The major fraction with a smaller R_f value on TLC was further separated by preparative HPLC into two alcohols, **23** and **25**. **23** seems to be D: B-friedo-18β,19αH-lup-5-en-3α-ol from the ^{1}H NMR spectrum: an olefinic proton at $C_{(6)}$ (δ 5.61, 1H, m, $W_{1/2}$=9 Hz) and $C_{(3\beta)}$-proton (δ 3.20, 1H, dd, J=10 and 4 Hz) attached to a hydroxyl-bearing carbon atom resembled those of D: B-friedo-olean-5-en-3α-ol (**24**)[12] (δ 5.63, 1H, m, $W_{1/2}$=9 Hz; δ 3.21, 1H, dd; J=10 and 5 Hz). **25** seems to be D : B-friedo-18β,19αH-lup-5(10)-en-3β-ol from a comparison of the ^{1}H NMR spectral data (δ 3.48, 1H, dd, J=10 and

4 Hz) with those of *D* : *B*-friedoolean-5(10)-en-3β-ol (**26**)[6b] (δ 3.45, 1H, dd; J=9.5 and 4.5 Hz) and *D* : *B*-friedobacchar-5(10)-en-3β-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-18β,19α*H*-lup-5(10)-en-3α-ol from the ^{1}H 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-18β,19α*H*-lup-5-en-3β-ol. However, yield was less than 3% from the bromide (**20**). No satisfactory characterization could be achieved.

Treatment of 3β,4β-epoxides of *D* : *A*-friedo-type triterpenes with boron trifluoride etherate gives a mixture of backbone-rearranged products, from which *D* : *B*-friedo-Δ^5- and -$\Delta^{5(10)}$-triterpene 3β-alcohols are obtained. For example, *D* : *B*-friedobacchar-5-en-3β-ol was obtained from 3β,4β-epoxyshionane[13] and *D*: *B*-friedoolean-5-en-3β-ol from 3β,4β-epoxyfriedelane[6b] together with their 5(10)-ene isomers, respectively. 3β,4β-Epoxy-*D* : *A*-friedo-18β,19α*H*-lupane (**17**) was treated with boron trifluoride etherate in benzene to give a complex mixture, from which an alcohol was obtained. The ^{1}H 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-18β,19α*H*-lup-5-en-3β-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-18β,19α*H*-lup-5-en-3-one (**21**), identical with that obtained by the oxidation of *D*: *B*-friedo-18β,19α*H*-lup-5-en-3α-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 ^{1}H 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-18β,19α*H*-lup-5-en-3β-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. ^{1}H 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)×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 GF_{254} (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-18β-lup-19-en-3β-yl Acetate (13).* Excess of sodium borohydride (*ca.* 10 mg) was added to a solution of *D*: *A*-friedo-18β-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-3β-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-3α-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-3β-ol (**26**)	191—193	δ 3.48 (1H, dd, J=10, J=4 Hz)	426 (M^+; 13%) 408 (100%) 205 (72%)
5(10)-en-3α-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-18β-lup-19-en-3β-ol (**12**; 7.2 mg) in 95% yield: mp 173—175 °C (crystallized from acetone); IR 3460 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8—1.0 (18H, 6×CH_3), 1.65 (6H, br s; >C=C(CH_3)$_2$), and 3.75 (1H, m, $W_{1/2}$=6 Hz); MS *m/e* 426 (M^+; 17) and 275 (100).

19-En-3β-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-18β-lup-19-en-3β-yl acetate (**13**; 6.8 mg) in 86% yield; mp 240—242.5 °C (crystallized from acetone); IR 1738 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.75—0.95 (18H, 6×CH_3), 1.63, 1.67 (each 3H, br s; >C=C(CH_3)$_2$), 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 $C_{32}H_{52}O_2$: C, 81.99; H, 11.18%.

D : A-*Friedo-18β,19α*H-*lupan-3β-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-18β,19α*H*-lupan-3β-yl acetate (**14**; 637 mg); mp 251—253 °C (crystallized from acetone); IR 1735 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8—1.0 (18H, 6×CH_3), 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 $C_{32}H_{54}O_2$: C, 81.64; H, 11.56%.

D : *A-Friedo-18β,19α*H-*lupan-3β-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-18β,19α*H*-lupan-3β-ol (**15**; 327 mg) in 97% yield; mp 225—227 °C (crystallized from acetone); IR 3440 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8—1.1 (24H, 8×CH_3) and 3.75 (1H, m, $W_{1/2}$= 7 Hz); MS *m/e* 428 (M^+; 100).

D : A-*Friedo-18β,19α*H-*lup-3-ene* (**16**). Freshly distilled phosphoryl chloride (1.8 ml) was added to a solution of 3β-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-18β,19α*H*-lup-3-ene (**16**; 254 mg) in 84% yield; mp 169—170 °C (crystallized from acetone); IR 795 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95—1.15 (21H, 7×CH_3), 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 $C_{30}H_{50}$: C, 87.73; H. 12.27%.

Epoxidation of D : A-*Friedo-18β,19α*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 3α,4α-epoxy-*D* : *A*-friedo-18β,19α*H*-lupane (**11**; 157.5 mg) and 3β,4β-epoxy-*D* : *A*-friedo-18β,19α*H*-lupane (**17**; 87.5 mg) in 60 and 33% yields, respectively. 3α,4α-Epoxy-*D* : *A*-friedo-18β,19α*H*-lupane (**11**): mp 200—202 °C (crystallized from acetone); ^1H NMR ($CDCl_3$) δ 0.85 (15H, 5×CH_3), 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 $C_{30}H_{50}O$: C, 84.44; H, 11.81%. 3β,4β-Epoxy-*D* : *A*-friedo-18β,19α*H*-lupane (**17**): mp 215—216 °C crystallized from acetone); ^1H NMR ($CDCl_3$) δ 0.88 (15H, 5×CH_3), 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 $C_{30}H_{50}O$: C, 84.44; H, 11.81%.

D : A-*Friedo-18β,19α*H-*lupan-3-one* (**18**). The 3β-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-18β,19α*H*-lupan-3-one (**18**; 236 mg) in 96% yield; mp 260—262 °C (crystallized from acetone); IR 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.72 (3H, s) and 0.8—1.0 (21H, 7×CH_3); ^1H NMR ($CDCl_3$) using Eu(fod)$_3$-d_{27}/**18**=0.2 (M/M) δ 1.72 (3H, d; *J*=7 Hz; 4β-CH_3); MS *m/e* 426 (M^+; 100); Found: C, 84.66; H, 11.79%. Calcd for $C_{30}H_{50}O$: C, 84.44; H, 11.81%.

3-Benzoyloxy-D : A-*friedo-18β,19α*H-*lup-3-ene* (**19**). *D*:*A*-friedo-18β,19α*H*-lupan-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-18β,19α*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 ($CDCl_3$) δ 0.9—1.0 (18H, 6×CH_3), 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 $C_{37}H_{54}O_2$: C, 83.72; H, 10.25%.

4α-Bromo-D : A-*friedo-18β,19α*H-*lupan-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 4α-bromo-*D* : *A*-friedo-18β,19α*H*-lupan-3-one (**20**; 31.6 mg) in 66% yield; mp 192.5—194.5 °C (crystallized from methanol); IR 1715 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8—1.0 (21H, 7×CH_3), 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 $C_{30}H_{49}O^{81}Br$: M, 506.2903. Found: *m/e* 504.2992. Calcd for $C_{30}H_{49}O^{79}Br$: M, 504.2967.

Dehydrobromination of 4α-Bromo-D : A-*friedo-18β,19α*H-*lupan-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 4α-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-18β,19α*H*-lup-5-en-3-one (**21**) and *D*:*B*-friedo-18β,19α*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.

Readuction 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 borhydride (*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-18β,19α*H*-lup-5-en-3α-ol (**23**) and *D*;*B*-friedo-18β,19α*H*-lup-5(10)-en-3β-ol (**25**), and the other

mixture (2.1 mg) with a larger R_f value consists of *D*: *B*-friedo-18β,19α*H*-lup-5-en-3β-ol (**10**) and *D*: *B*-friedo-18β,19α*H*-lup-5(10)-en-3α-ol (**28**). The former mixture was separated by preparative HPLC into *D*: *B*-friedo-18β,19α*H*-lup-5-en-3α-ol (**23**; 5.2 mg) and *D*:*B*-friedo-18β,19α*H*-lup-5(10)-en-3β-ol (**25**; 9.8 mg). *D*: *B*-Friedo-18β,19α*H*-lup-5-en-3α-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$\times CH_3$), 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 $C_{30}H_{50}O$: M, 426.3860. *D*: *B*-Friedo-18β,19α*H*-lup-5(10)-en-3β-ol (**25**); mp 191—193 °C (crystallized from acetone); IR 3350 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.8—1.05 (24H, 8$\times CH_3$) 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 $C_{30}H_{50}O$: M, 426.3860.

The latter mixture of **10** and **28** was separated by preparative HPLC into *D*: *B*-friedo-18β,19α*H*-lup-5-en-3β-ol (**10**; less than 0.5 mg) and -5(10)-en-3α-ol (**28**; 1.1 mg). *D*: *B*-Friedo-18β,19α*H*-lup-5(10)-en-3α-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, ($C\underline{H}_3$)$_2$CH–), 0.97, 1.03 (each 3H, s), 0.89, 1.00 (each 6H, s, 2$\times CH_3$), 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 $C_{30}H_{50}O$: M, 426.3860.

Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 3β,4β-Epoxy-D:A-*friedo-18β,19α*H*-lupane (17) in Benzene.* A solution of 3β,4β-epoxy-*D*:*A*-friedo-18β,19α*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-18β,19α*H*-lupan-3-one (**18** 0.5 mg), *D*: *B*-friedo-18β,19α*H*-lup-5-en-3β-ol (**10**; 4.4 mg), and a complex mixture of alcohols (37.2 mg). *D*: *B*-Friedo-18β,19α*H*-lup-5-en-3β-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*-CH_3), 0.90 (6H, d; J=6 Hz; ($C\underline{H}_3$)$_2$CH–), 0.97 (6H, s, 2$\times$*t*-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 $C_{30}H_{50}O$: M, 426.3860.

D: B-*Friedo-18β,19α*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-18β,19α*H*-lup-5-en-3α-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-18β,19α*H*-lup-5-en-3-one (**21**; 1.6 mg).

b): The same oxidation of *D*: *B*-friedo-18β,19α*H*-lup-5-en-3β-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; ($C\underline{H}_3$)$_2$CH–), 1.21 (12H, s, 4$\times CH_3$), 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 $C_{30}H_{48}O$: M, 424.3705.

D: B-*Friedo-18β,19α*H*-lup-5(10)-en-3-one (22).* *a)*: Pyridinium chlorochormate[14] (16 mg) was added to a solution of *D*: *B*-friedo-18β,19α*H*-lup-5(10)-en-3α-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-18β,19α*H*-lup-5(10)-en-3-one (**22**; 10.1 mg).

b): A solution of *D*: *B*-friedo-18β,19α*H*-lup-5(10)-en-3β-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$\times CH_3$), 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 $C_{30}H_{48}O$: M, 424.3705.

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