Migrated Lupane Derivatives. Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 3α,4α- and 3β,4β-Epoxy-*D*:*A*-friedo-18β,19α*H*-lupanes and Solvent Effects[1)]

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Backbone rearrangements of 3α,4α- and 3β,4β-epoxy-*D*:*A*-friedo-18β,19α*H*-lupanes catalyzed by boron trifluoride etherate gave 18β,19α*H*-lup-12-en-3-ols, lup-18-en-3-ols, and lup-19-en-3-ols, besides known *D*:*B*-friedo-18β,19α*H*-lup-5-en-3-ols and -5(10)-en-3-ols. *D*:*B*-Friedo-18β,19α*H*-lup-1(10)-en-3α-ol and 3β,10β-epoxy-*D*:*B*-friedo-18β,19α*H*-lupane were also obtained from α- and β-epoxides, respectively. Solvent effects on these reactions were examined.

Acid-catalyzed backbone rearrangements of unsaturated or epoxy triterpenes usually proceed in a reverse direction of their biogenesis,[2)] affording a number of migrated triterpenes derived from intermediate cations or their equivalent species corresponding to various biogenetic stages. In previous papers, reports were given on boron trifluoride etherate-catalyzed backbone rearrangement of 3β,4β-epoxyfriedelane (**1**)[3)] and 3α, 4α- and 3β,4β-epoxyshionanes (**2** and **3**),[4)] migrated friedooleanane and friedobaccharane derivatives being obtained.

So far only a few migrated lupane derivatives have been isolated from natural sources,[5)] investigations on these compounds[6,7)] not being as extensive as those on migrated oleanane, ursane, and hopane derivatives.[8)] In connection with the structural study of guimarenol, formation of *D*:*B*-friedo-18β,19α*H*-lup-5-en-3β-ol from 3β,4β-epoxy-*D*:*A*-friedo-18β,19α*H*-lupane by tratment with boron trifluoride etherate in benzene has been reported.[9)] Examination was carried out on the backbone rearrangement of 3α,4α- and 3β,4β-epoxy-*D*:*A*-friedo-18β,19α*H*-lupanes[9)] (**4** and **5**) in various solvents catalyzed by boron trifluoride etherate to give a series of migrated lupane derivatives. Solvent effects on the reaction were also examined.

3α,4α-Epoxy-*D*:*A*-friedo-18β,19α*H*-lupane (**4**), derived from friedelin (friedelan-3-one)[7,9)] was treated with boron trifluoride etherate in tetrahydrofuran at room temperature until the epoxide (**4**) was consumed. The reaction give a complex mixture, which was separated by preparative thin-layer chromatography (TLC), followed by column chromatography on silica gel impregnated with silver nitrate to afford three compounds **A**, **B**, and **C** in 11, 60, and 5% yields, respectively.

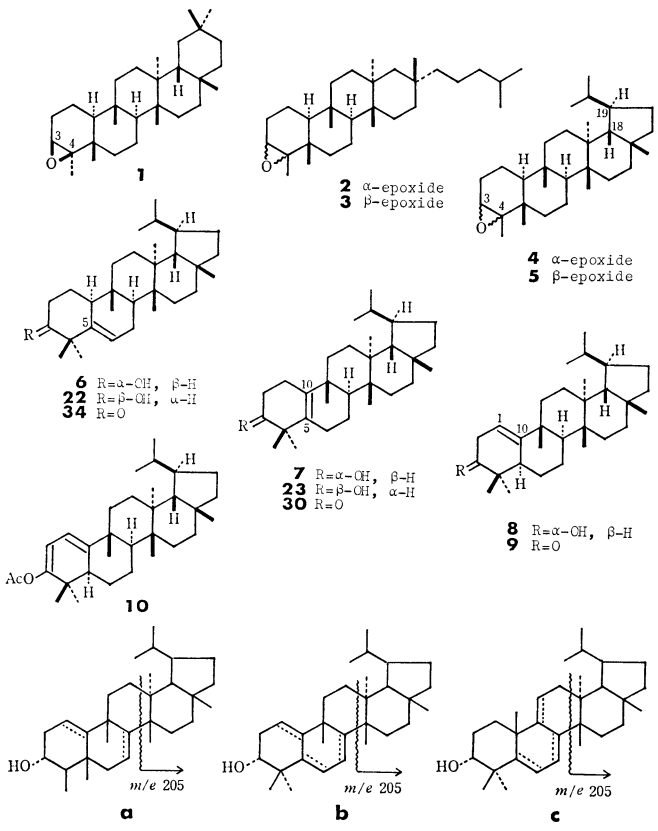
The most polar compound **A** was found to be *D*:*B*-friedo-18β,19α*H*-lup-5-en-3α-ol (**6**) and the less polar compound **B** *D*:*B*-friedo-18β,19α*H*-lup-5(10)-en-3α-ol (**7**) by comparison with authentic specimens.[9)]

Spectral data [IR 3400 and 908 cm^{-1}; ^1H NMR δ 3.34 (1H, m) and 5.22 (1H, m)] showed the least polar compound **C**, $C_{30}H_{50}O$, mp 103—109 °C, to be a new alcohol with a trisubstituted double bond. A fragment ion peak at *m/e* 205 in the mass spectrum[10)] indicates that the double bond should be located at $\Delta^{1(10)}$ or Δ^7 of a *D*:*A*-friedolupane framework (**a**), $\Delta^{1(10)}$, Δ^5, or Δ^7 of a *D*:*B*-friedolupane framework (**b**), or Δ^5, Δ^7, or $\Delta^{9(11)}$ of a *D*:*C*-friedolupane framework (**c**). Among them, alcohols with the *D*:*A*-friedo-type framework, *D*:*B*-friedo-Δ^7-type framework, and *D*:*C*-friedo-Δ^5-type framework are not feasible on the basis of their formation mechanism. 5-En-3α-ol with the *D*:*B*-friedo-type framework is compound (**6**). Thus compound **C** should be formulated as either *D*:*B*-friedo-18β,19α*H*-lup-1(10)-en-3α-ol (**8**), *D*:*C*-friedo-18β,19α*H*-lup-7-en-3α-ol, or -9(11)-en-3α-ol.

Oxidation of compound **C** with the Jones reagent gave an unsaturated ketone (**9**), $C_{30}H_{48}O$, IR 1710 cm^{-1}. In the ^1H NMR spectrum, allylic methylene protons resonate at δ 2.75 and 3.01 (each 1H, dt, J=21 and J=3 Hz) and an olefinic proton at δ 5.43 (1H, m). Furthermore, another allylic proton resonates at δ 2.35 (1H, m). These observations suggest the existence of a partial structure $-\overset{\overset{O}{\|}}{C_{(3)}}-C_{(2)}H_2-C_{(1)}H=\overset{|}{C_{(10)}}-\overset{|}{C_{(5)}}H-$ and *D*:*B*-friedo-18β,19α*H*-lup-1(10)-en-3-one for the unsaturated ketone (**9**). On irradiation at δ 5.43, the signal due to the methylene at $C_{(2)}$ turned into two pairs of double doublet signals (each 1H, J=21 and J=3 Hz), showing that the coupling constant values between the $C_{(1)}$-proton and the $C_{(2)}$-methylene protons are both 3 Hz, and the $C_{(2)}$-protons coupled with the $C_{(5)}$-methine proton with a coupling constant, J=3 Hz. Irradiation of a frequency around δ 2.9 due to the $C_{(2)}$-methylene protons resulted in the change of the signal of $C_{(1)}$-proton to a doublet signal (1H, J=2 Hz). This suggests that the coupling constant between the olefinic proton and the $C_{(5)}$-allylic methine proton is 2 Hz. When the signal around δ 2.35 was irradiated, the signal at δ 5.43 due to the $C_{(1)}$-proton turned to a triplet (1H, J=3 Hz).

Treatment of the β,γ-unsaturated ketone (**9**) with isopropenyl acetate in the presence of *p*-toluenesulfonic acid under reflux gave a conjugated dienol acetate (**10**) [UV 273 nm (ε *ca.* 8000); $C_{32}H_{50}O_2$]. Thus, the structure of *D*:*B*-friedo-18β,19α*H*-lup-1(10)-en-3α-ol (**8**) is given for compound **C**.

Reaction of the α-epoxide (**4**) with boron trifluoride etherate in benzene at room temperature gave *D*:*B*-friedo-18β,19α*H*-lup-5(10)-en-3α-ol (**7**; yield 34%), -5-en-3α-ol (**6**; trace), and an alcohol mixture **D**. The mixture showed two peaks on GLC, but could not



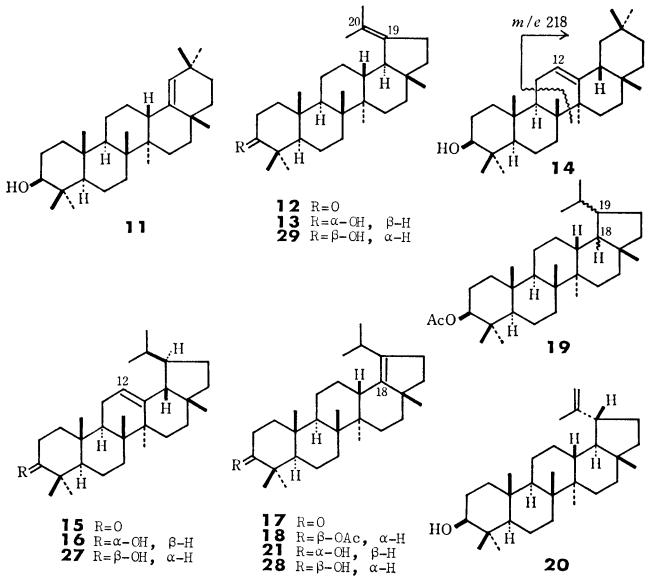
be separated by TLC nor column chromatography. Oxidation of the mixture with the Jones reagent gave the corresponding ketone mixture, which was separable by high performance liquid chromatography (HPLC) to afford three compounds, $\mathbf{D}_1$, $\mathbf{D}_2$, and $\mathbf{D}_3$ in 3, 11, and 6% yields, respectively.

The compound $\mathbf{D}_1$, $C_{30}H_{48}O$, is a ketone with an isolated double bond, the ^{1}H NMR spectrum showing the presence of two olefinic methyls besides six tertiary methyls. No signal due to olefinic proton was observed. From the fact that germanicol (**11**) was obtained as an ultimate product in friedelane-oleanane rearrangement in benzene,[3b] the compound $\mathbf{D}_1$ should be formulated as lup-19-en-3-one (**12**) in accordance with the ^{1}H NMR spectral data. The original alcohol in the mixture **D** could be formulated as lup-19-en-3α-ol (**13**).

The compound $\mathbf{D}_2$ showed a molecular ion peak at *m/e* 424.3708 ($C_{30}H_{48}O$) and a prominent peak at *m/e* 218.2004 corresponding to a fragment ion $C_{16}H_{26}^+$. Since Δ^{12}-triterpenes such as β-amyrin (**14**), α-amyrin, and bacchar-12-en-3-one show a prominent peak at *m/e* 218 due to retro-Diels-Alder fragmentation,[11] compound $\mathbf{D}_2$ might be 18β,19αH-lup-12-en-3-one (**15**). The proposed structure is supported by its ^{1}H NMR spectrum; a signal due to an olefinic proton observed at δ 5.21 (t, J=4 Hz) is nearly the same as that (δ 5.20, t, J=4 Hz) of β-amyrin (**14**). The original alcohol should be represented as 18β, 19αH-lup-12-en-3α-ol (**16**).

The third compound $\mathbf{D}_3$, $C_{30}H_{48}O$, mp 167—168 °C, was found to be a tetrasubstituted olefinic ketone by its ^{1}H NMR spectrum which showed the absence of the olefinic proton and the presence of an allylic proton (δ 2.98, 1H, J=6 Hz). The signal resonating at δ 2.98 seems to be central three peaks of a heptet signal due to an isopropyl methine proton on the allylic position. Thus the structure of lup-18-en-3-one (**17**) is suggested for compound $\mathbf{D}_3$.

We prepared a mixture of lup-18-en-3β-yl acetate (**18**) and 18ξ,19ξH-lupan-3β-yl acetate (**19**) from lupeol (**20**) according to the method of Baddeley *et al.*[12] The mixture was treated with lithium aluminium hydride to give an alcohol mixture, which was oxidized with the Jones reagent. The reaction mixture was subjected to separation by HPLC to afford the authentic lup-18-en-3-one (**17**), which was identical with compound $\mathbf{D}_3$. Thus the original alcohol is formulated as lup-18-en-3α-ol (**21**).



The reactions of 3β,4β-epoxy-*D*:*A*-friedo-18β,19αH-lupane (**5**), derived from friedelin,[7,9] with boron trifluoride etherate were investigated under the same conditions as in the case of the α-epoxide (**4**). Treatment of the β-epoxide (**5**) in tetrahydrofuran gave a mixture which was separated into three compounds, **E**, **F**, and **G** in 7, 40, and 11% yields, respectively. The most polar compound **E** and the less polar one **F** were identified as *D*:*B*-friedo-18β,19αH-lup-5-en-3β-ol (**22**) and -5(10)-en-3β-ol (**23**) by direct comparison with authentic samples,[9] respectively.

The least polar compound **G**, mp 171 °C, seems to be a fluorohydrin (**24**). Its ^{1}H NMR spectrum showed a multiplet signal centered at δ 3.68 (1H, $W_{1/2}$=13 Hz) due to a proton on a carbon atom bearing a hydroxyl group. A doublet signal appearing at δ 1.33 (J=24 Hz) indicates the presence of a methyl group attached to a fluorine-bearing carbon atom. The coupling constant value, $J_{F,H}$=24 Hz, is the same as that ($J_{F,H}$= 24 Hz) observed for 4α-fluoroshionan-3β-ol (**25**).[4b] The mass spectrum showed a molecular ion peak at *m/e* 446 (1%) and a characteristic peak at *m/e* 426 (8%) due to $(M-HF)^+$ ion together with a base peak at *m/e* 123. The results together with the fact that a fluorohydrin is often generated by treatment of an

epoxide with boron trifluoride etherate,[3,4b] lead to the conclusion that compound **G** can be formulated as 4α-fluoro-*D*:*A*-friedo-18β,19α*H*-lupan-3β-ol (**24**).

The reaction of β-epoxide (**5**) in benzene gave three products, *D*:*A*-friedo-18β,19α*H*-lupan-3-one (**26**: yield 1%),[9] a fluorohydrin (**24**; yield 13%), and *D*:*B*-friedo-18β,19α*H*-lup-5-en-3β-ol (**22**; yield 9%), other than an alcohol mixture (**27**—**29**) as main products. The mixture, after oxidation with the Jones reagent, was separated by HPLC to afford *D*:*B*-friedo-18β,19α*H*-lup-5(10)-en-3-one[9] (**30**; yield 7%), lup-19-en-3-one (**12**; yield 7%), 18β,19α*H*-lup-12-en-3-one (**15**; yield 31%), and lup-18-en-3-one (**17**; yield 13%).

The reaction of β-epoxide (**5**) in diethyl ether was carried out at 0 °C for 20 min. The reaction mixture was separated by preparative TLC into five compounds. The least polar compound **H** (**31**; yield 22%), $C_{30}H_{50}O$, mp 136—138 °C, showed no characteristic absorption bands in its IR spectrum. A doublet signal at δ 3.72 (1H, J=5.5 Hz), resembling a characteristic signal due to $C_{(3)}$-proton of dendropanoxide (**32**)[3a] (δ 3.75, 1H, d, J=4.8 Hz) and of dihydrobaccharis oxide (**33**)[4b] (δ 3.73, 1H, d, J=5 Hz), was observed in the ^{1}H NMR spectrum. Thus compound **H** was confirmed to be 3β,10β-epoxy-*D*:*A*-friedo-18β,19α*H*-lupane (**31**). The other four compounds were found to be *D*:*A*-friedo-18β,19α*H*-lupan-3-one (**26**; yield 2%), a fluorohydrin (**24**; yield 20%), *D*:*B*-friedo-18β,19α*H*-lup-5-en-3β-ol (**22**; yield 11%), and -5(10)-en-3β-ol (**23**; yield 27%) by spectral data and comparison with authentic specimens.

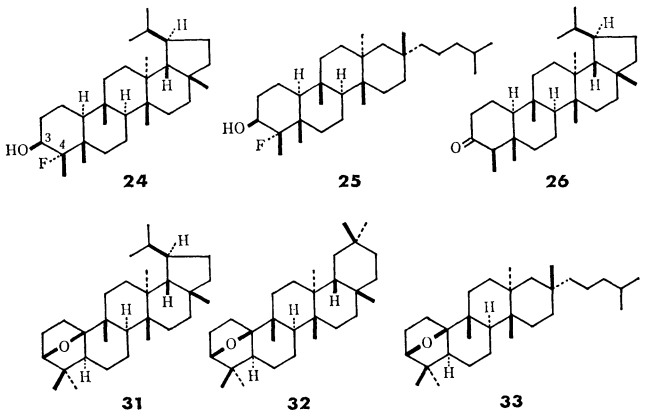


Table 1. Relative amount ratios of products in the reaction of 3α,4α-epoxide (**4**) with BF_3·OEt_2 at room temperature[a]

Solvent	Time / min	5-ene (**6**)	5(10)-ene (**7**)	1(10)-ene (**8**)	12-ene (**16**)	18-ene (**21**)	19-ene (**13**)
Hexane[b]	30	8	18	0	40	24	10
CH_3CN[b]	30	6	13	0	34	13	34
Benzene	60	trace[c]	63[c]	0	20[d]	11[d]	6[d]
CH_2Cl_2[b]	30	3	46	0	29	16	6
DME[b]	30	17	67	12	2	trace	2
Ether[b]	30	15	76	3	2	1	3
THF	45	15[c]	78[c]	7[c]	0	0	0

a) Room temperature, 20—28 °C. b) Determined by small-scale experiments, reaction products being subjected to Jones oxidation. Relative yields of 1(10)-, 12-, 18-, and 19-enes estimated from the peak area of the corresponding ketones on HPLC under the conditions given in General. A mixture containing *D*:*B*-friedo-18β,19α*H*-lup-5-en-3-one (**34**) and -5(10)-en-3-one (**30**) was separated by HPLC and examined by GLC to determine relative yields of 5- and 5(10)-enes. c) Determined by isolation of the product. d) Determined by conversion of the product into the corresponding ketone, isolated by means of preparative HPLC.

Table 2. Relative amount ratios of products in the reaction of 3β,4β-epoxide (**5**) with BF_3·OEt_2 at room temperature[a]

Solvent	Time / min	(**26**)[b]	(**25**)[b]	5-ene (**22**)	5(10)-ene (**23**)	(**31**)	12-ene (**27**)	18-ene (**28**)	19-ene (**29**)
Hexane[c]	60	trace	trace	21	22	0	23	10	24
CH_3CN[c]	60	0	7	11	38	0	27	9	8
Benzene	60	2[d]	4[d]	13[d]	10[e]	0	43[e,f]	18[e,f]	10[e]
CH_2Cl_2[c]	60	0	3	25	33	0	16	14	9
DME[c]	60	0	0	26	67	2	2	1	2
Ether[g]	20	3[d]	25[d]	13[d]	33[d]	26[d]	0	0	0
THF	45	0	19[d]	12[d]	69[d]	0	0	0	0

a) Room temperature, 20—28 °C. b) Determined by GLC before oxidation for small-scale experiments. c) Determined by small-scale experiments, reaction products being subjected to Jones oxidation. Relative yields of 1(10)-, 12-, 18-, and 19-enes estimated from the peak area of the corresponding ketones on HPLC under the conditions given in General. A mixture containig *D*:*B*-friedo-18β,19α*H*-lup-5-en-3-one (**34**) and -5(10)-en-3-one (**30**) was separated by HPLC and examined by GLC to determine relative yields of 5- and 5(10)-enes. d) Determined by isolation of the product. e) Determined by conversion of the product into the corresponding ketone, isolated by means of preparative HPLC. f) Correct data, inverse data in preliminary report (Ref. 1). g) Reaction carried out at 0 °C.

Small-scale experiments using the 3α,4α-epoxide (**4**) or the 3β,4β-epoxide (**5**) (each *ca.* 10 mg) and boron trifluoride etherate (0.1 ml) were carried out in solvents (5—10 ml) such as hexane, dichloromethane, acetonitrile, and 1,2-dimethoxyethane (DME). The results together with those obtained for the reactions in other solvents are summarized in Tables 1 and 2.

Since the rearrangement of **4** and **5** in a solvent with low nucleophilicity proceeds up to the C, D, or E ring,[3,4] highly rearranged products with 12-ene, 18-ene, and 19-ene structures were obtained in the reaction in hexane, acetonitrile, benzene, and dichloromethane. On the other hand, the rearrangement in a solvent with high nucleophilicity, such as diethyl ether or tetrahydrofuran, was interrupted in an early stage to afford *D*:*A*-friedolupane derivatives or *D*:*B*-friedolup-5-ene and -5(10)-ene derivatives. Neither *D*:*C*-friedolup-7-ene nor -8-ene derivative was detected in any solvent. These migratory aptitudes have a strong resemblance to those observed for 3β,4β-epoxyfriedelane (**1**)[3b] of a *D*:*A*-friedooleanane-type rather than those for 3α,4α- and 3β,4β-epoxyshionanes (**2** and **3**)[4b] of a *D*:*A*-friedobaccharane-type. The difference may be due to the existence of the E ring; the fact that the rearrangements of **1**, **4**, and **5** do not stop at the stages giving the *D*:*C*-friedo-type derivatives, but proceed up to the D and E rings, may be explained by release of the intracyclic tension due to the *cis*-fused D/E ring and partly due to 1,3-diaxial methyl groups.

A series of migrated lupanes were thus derived from friedelin. Since the total synthesis of friedelin has been accomplished,[13] the present work constitutes formally the total synthesis of these migrated lupanes.

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, UV spectra with a Hitachi 340 spectrophotometer, mass spectra with a Hitachi RMU-6-Tokugata mass spectrometer at 70 eV with a direct inlet system, high resolution mass spectra with a JMS-D300 (JEOL) mass spectrometer, the relative intensity being given in parentheses, and ^{1}H NMR spectra with a Hitachi R-20B (60 MHz) spectrometer, a Varian EM-390 (90 MHz) spectrometer or a JNM-FX-60 FT-NMR (60 MHz) spectrometer (JEOL). Chemical shifts are expressed in δ downfield from TMS as an internal standard and coupling constants in Hz. GLC analysis was carried out on a Shimadzu Gas Chromatograph GC-6A equipped with a hydrogen flame ionization detector (column: Dexsil 300GC, temperature 270—290 °C). Analytical and preparative HPLC 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; flow rate: 3 ml/min; pressure: 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 silica gel column chromatography.

Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 3α,4α-Epoxy-D:A-*friedo-18β,19α*H*-lupane (**4**) in Tetrahydrofuran.* A solution of α-epoxide[9] (**4**; 84.0 mg) in tetrahydrofuran (20 ml) was treated with freshly distilled boron trifluoride etherate (0.5 ml) at room temperature for 45 min. A saturated aqueous sodium hydrogencarbonate solution (5 ml) was added, stirring being continued for 30 min. The usual work-up gave a mixture, which was separated by preparative TLC (developed with benzene–diethyl ether, 19:1) to afford *D*:*B*-friedo-18β,19α*H*-lup-5(10)-en-3α-ol[9] (**7**; 50.0 mg) and crude 1(10)-en-3α-ol (**8**) and 5-en-3α-ol[9] (**6**). The crude alcohol (**8**) was further purified by column chromatography on silica gel impregnated with 25% silver nitrate. Elution with benzene gave pure **8** (4.3 mg). The crude alcohol (**6**) was subjected to further separation by preparative TLC (developed with benzene–diethyl ether, 19:1) to give pure **6** (9.6 mg). **8**: mp 103—109 °C (crystallized from methanol); IR 3400 and 908 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.63, 0.82, 1.01, 1.10 (each 3H, s), 0.89 (6H, d, J=6 Hz; ($C\underline{H}_3$)$_2$CH–), 0.96 (6H, s), 3.34 (1H, m, $W_{1/2}$=7 Hz), and 5.22 (1H, m, $W_{1/2}$=8 Hz); MS *m/e* (%) 426 (M^+; 41), 408 (100), and 205 (40); Found: *m/e* 426.3847. Calcd for $C_{30}H_{50}O$: M, 426.3860.

D:B-*Friedo-18β,19α*H*-lup-1(10)-en-3-one (**9**).* The Jones reagent (one drop) was added to a solution of **8** (7.0 mg) in acetone (5 ml) at 0 °C, and the reaction mixture was stirred at 0 °C for 20 min. The usual work-up gave a residue (6.9 mg), which was purified by preparative TLC (developed with benzene) to afford *D*:*B*-friedo-18β,19α*H*-lup-1(10)-en-3-one (**9**; 4.1 mg), mp 215—218 °C (crystallized from acetone); IR 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.8—0.95 (9H, 3×CH_3), 0.96, 0.99, 1.01, 1.08, 1.15 (each 3H, s), 2.35 (1H, m), 2.75 (1H, dt, J=21 and J=3 Hz), 3.01 (1H, dt, J=21 and J=3 Hz), and 5.43 (1H, m, $W_{1/2}$=9 Hz); MS *m/e* (%) 424 (M^+; 55), 205 (100), and 123 (86); Found: *m/e* 424.3710. Calcd for $C_{30}H_{48}O$: M, 424.3705.

3-Acetoxy-D:B-*friedo-18β,19α*H*-lupa-1(10),2-diene (**10**).* A mixture of **9** (0.7 mg), isopropenyl acetate (2 ml), and *p*-toluenesulfonic acid (catalytic amount) was refluxed for 10 h. The usual work-up gave a residue, which was purified by preparative TLC (developed with benzene) to give 3-acetoxy-*D*:*B*-friedo-18β,19α*H*-lupa-1(10),2-diene (**10**; 0.1 mg), UV_{max} (dioxane) 273 nm (ε *ca.* 8000); MS *m/e* (%) 466 (M^+; 4) and 123 (100); Found: *m/e* 466.3822. Calcd for $C_{32}H_{50}O_2$: M, 466.3811.

Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 3α,4α-Epoxy-D:A-*friedo-18β,19α*H*-lupane (**4**) in Benzene.* A solution of α-epoxide (**4**; 30.1 mg) in benzene (15 ml) was treated with boron trifluoride etherate (0.3 ml) at room temperature for 1 h. A saturated aqueous sodium hydrogencarbonate solution (10 ml) was added, stirring being continued for 20 min. The usual work-up gave a mixture, which was subjected to separation by preparative TLC (developed with benzene–diethyl ether, 9:1) to afford *D*:*B*-friedo-18β,19α*H*-lup-5(10)-en-3α-ol (**7**; 10.1 mg), -5-en-3α-ol (**6**; trace), and a mixture (9.7 mg) of alcohols. This mixture, dissolved in acetone (5 ml), was oxidized with the Jones reagent (one drop) at 0 °C, and the solution was stirred at 0 °C for 1 h. After the usual work-up, the reaction mixture was purified by preparative TLC (developed with benzene) to give a mixture (7.7 mg) of 3-oxo compounds. The mixture was separated by preparative HPLC into lup-19-en-3-one (**12**; 1.0 mg), 18β,19α*H*-lup-12-en-3-one (**15**; 3.2 mg), and lup-18-en-3-one (**17**; 1.8 mg). **12**: mp 174—177 °C (crystallized from acetone); IR 1712 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.77, 0.91, 0.95, 1.06 (each 3H, s), 1.01 (6H, s; 2×CH_3), 1.53 and 1.55 (each 3H, s; >C=C(CH_3)$_2$); MS *m/e* (%) 424 (M^+; 65) and 257 (100); Found: *m/e* 424.3711. Calcd for $C_{30}H_{48}O$: M, 424.3705. HPLC R_t=28.8 min.

15: mp 152.5—153 °C (crystallized from acetone); IR 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77, 0.87 (each 3H, d, J= 6 Hz), 0.94, 1.01 (each 3H, s), 1.07, 1.13 (each 6H, s; 2× CH_3), and 5.21 (1H, t, J=4 Hz); MS *m/e* (%) 424 (M^+; 100) and 218 (88); Found: *m/e* 424.3708. Calcd for $C_{30}H_{48}O$: M, 424.3705. HPLC R_t=31.3 min. **17**: mp 167—168 °C (crystallized from acetone); IR 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.82—1.05 (21H; 7×CH_3), and 1.07 (3H, s); MS *m/e* (%) 424 (M^+; 100); Found: *m/e* 424.3691. Calcd for $C_{30}H_{48}O$: M, 424.3705. HPLC R_t=32.2 min.

Preparation of Lup-18-en-3-one (17). A mixture[12] (32.4 mg) of lup-18-en-3β-yl acetate (**18**) and 18ξ,19ξ*H*-lupan-3β-yl acetate (**19**) was dissolved in tetrahydrofuran (20 ml), and treated with lithium aluminium hydride (51 mg) under reflux for 2 h. The usual work-up gave a mixture (34.0 mg) of lup-18-en-3β-ol and 18ξ,19ξ*H*-lupan-3β-ol. A portion (17 mg) of this mixture was dissolved in acetone, a drop of the Jones reagent being added at 0 °C. After the reaction mixture had been stirred for 50 min, the usual treatment gave a residue, which was subjected to separation by preparative HPLC to afford lup-18-en-3-one (**17**; 8.9 mg).

Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 3β,4β-Epoxy-D:A-*friedo-18β,19α*H*-lupane (5) in Tetrahydrofuran.* A solution of β-epoxide[9] (**5**; 31.2 mg) in tetrahydrofuran (15 ml) was treated with freshly distilled boron trifluoride etherate (0.3 ml) at room temperature for 45 min. The same work-up as in the case of α-epoxide (**4**) gave a mixture, which was separated by preparative TLC (developed with benzene–diethyl ether, 9:1) to give *D:B*-friedo-18β,19α*H*-lup-5(10)-en-3β-ol[9] (**23**; 12.4 mg) and a mixture (7.3 mg) of 5-en-3β-ol[9] (**22**) and 4α-fluorohydrin (**24**). The mixture was subjected to separation by column chromatography on silica gel impregnated with 25% silver nitrate. Elution with benzene gave **24** (3.3 mg) and **22** (2.2 mg). **24**: mp 171 °C (crystallized from methanol); IR 3470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84—0.93 (15H; 5×CH_3), 1.07, 1.25 (each 3H, s), 1.33 (3H, d, J=24 Hz), and 3.68 (1H, m, $W_{1/2}$=13 Hz); MS *m/e* (%) 446 (M^+; 1), 426 (8), and 123 (100); Found: *m/e* 446.3935. Calcd for $C_{30}H_{51}OF$: M, 446.3924.

*Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 3β,4β-Epoxy-D:A-friedo-18β,19α*H*-lupane (5) in Benzene.* A solution of β-epoxide (**5**; 47.0 mg) in benzene (25 ml) was treated with boron trifluoride etherate (0.3 ml) at room temperature for 1 h. The same work-up gave a mixture, which was subjected to separation by preparative TLC (developed with benzene) to afford *D:A*-friedo-18β,19α*H*-lupan-3-one[9] (**26**; 0.5 mg), 4α-fluoro-*D:A*-friedo-18β,19α*H*-lupan-3β-ol (**24**; 1.5 mg), *D:B*-friedo-18β,19α*H*-lup-5-en-3β-ol (**22**; 4.4 mg), and a mixture (37.2 mg) of alcohols (**27**—**29**). This mixture was dissolved in acetone (10 ml), the Jones reagent (3 drops) being added at 0 °C. The solution was stirred at 0 °C for 15 min. After the usual treatment, the residue was purified by preparative TLC (developed with benzene) to afford a mixture (31.9 mg) of 3-oxo compounds, which was separated by preparative HPLC into *D:B*-friedo-18β,19α*H*-lup-5(10)-en-3-one[9] (**30**; 3.4 mg), lup-19-en-3-one (**12**; 3.5 mg), 18β,19α*H*-lup-12-en-3-one (**15**; 14.5 mg), and lup-18-en-3-one (**17**; 6.2 mg).

Boron Trifluoride Etherate-catalyzed Backbone Rearrangement of 3β,4β-Epoxy-D:A-*friedo-18β,19α*H*-lupane (5) in Diethyl Ether.* A solution of β-epoxide (**5**; 41.8 mg) in diethyl ether (20 ml) was treated with boron trifluoride etherate (0.4 ml) for 20 min at 0 °C. A saturated aqueous sodium hydrogencarbonate solution (10 ml) was added, stirring being continued for 20 min. The usual work-up gave a mixture, which was separated by preparative TLC (developed with benzene) to afford 3β,10β-epoxy-*D:B*-friedo-18β,19α*H*-lupane (**31**; 9.0 mg), *D:A*-friedo-18β,19α*H*-lupan-3-one (**26**; 1.0 mg), 4α-fluoro-*D:A*-friedo-18β,19α*H*-lupan-3β-ol (**24**; 8.7 mg), *D:B*-friedo-18β,19α*H*-lup-5-en-3β-ol (**22**; 4.6 mg), and -5(10)-en-3β-ol (**23**; 11.4 mg). **31**: mp 136—138 °C (crystallized from acetone); ^1H NMR ($CDCl_3$) δ 0.84—1.03 (18H; 6× CH_3), 1.67 (6H, s; 2×CH_3), and 3.72 (1H, d, J=5.5 Hz); MS *m/e* (%) 426 (M^+; 79) and 411 (100); Found: *m/e* 426.3861. Calcd for $C_{30}H_{50}O$: M, 426.3860.

Solvent Effects on the Backbone Rearrangement of 3α,4α-Epoxy-D:A-*friedo-18β,19α*H*-lupane (4).* Five portions of α-epoxide (**4**; each *ca.* 10 mg) were dissolved in hexane (5 ml), dichloromethane (5 ml), acetonitrile (10 ml), diethyl ether (5 ml), and 1,2-dimethoxyethane (5 ml), respectively, each solution being treated with boron trifluoride etherate (0.1 ml) at room temperature for 30 min. A residue, obtained after the usual work-up, was dissolved in acetone (5 ml) and treated with the Jones reagent (0.1 ml) at 0 °C for 1 h. After purification by preparative TLC (developed with benzene), a mixture of the 3-oxo compounds was examined by HPLC. Since *D:B*-friedo-18β,19α*H*-lup-5-en-3-one[9] (**34**) and -5(10)-en-3-one (**30**) showed the same retention time (R_t=27.3 min) under these conditions, a fraction with R_t=27.3 min was separated by HPLC, the relative amounts of two compounds, **34** (R_t=14.3 min) and **30** (R_t= 12.3 min) being examined by GLC.

Solvent Effects on the Backbone Rearrangement of 3β,4β-Epoxy-D:A-*friedo-18β,19α*H*-lupane (5).* Four portions of β-epoxide (**5**; each *ca.* 10 mg) were dissolved in hexane (5 ml), dichloromethane (5 ml), acetonitrile (10 ml), and 1,2-dimethoxyethane (5 ml), respectively, each solution being treated with boron trifluoride etherate (0.1 ml) at room temperature for 1 h. A part of the residue, obtained by the usual treatment, was examined by GLC to determine the relative amount ratios of 4α-fluoro-*D:A*-friedo-18β,19α*H*-lupan-3β-ol (**24**; R_t=19.9 min), 3β,10β-epoxy-*D:B*-friedo-18β,19α*H*-lupane (**31**; R_t=9.6 min), and *D:A*-friedo-18β,19α*H*-lupan-3-one (**26**; R_t=16.5 min). The remaining part of the residue was oxidized with the Jones reagent (0.1 ml) in acetone (5 ml) at 0 °C for 1 h, the oxidized product being purified by preparative TLC (developed with benzene). Relative amount ratios of the 3-oxo compounds were estimated in the same way as in the case of α-epoxide (**4**).

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