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EPOXIDATION REACTION OF 6β-ACETOXYEUDESMENES AND ACID-CATALYZED TRANSFORMATIONS OF THE EPOXY COMPOUNDS

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ABSTRACT.—A study of the epoxidation of 6β-acetoxyeudesm-3-enes, -4-enes, and -4(15)-enes has been performed. On some occasions, participation of the 6β acetoxy group has been observed. Treatment of the epoxy compounds in an acidic medium of pyridinium *p*-toluene sulfonate yielded several products of rearrangement and ring opening of the starting epoxy compounds. The determination of the stereochemistry of all the compounds and, particularly, the stereochemistry of C-4 were achieved principally by nOe difference experiments.

The epoxidation of eudesm-3-ene, -4-ene, and -4(15)-ene has not been studied in a systematic form, although there are some precedents (1,2) asserting that epoxidation occurs from the α side of the systems. Nevertheless, Bohlmann *et al.* (3) indicated that the formation of epoxides in nonlactonic eudesmenes with a 6β sustituent occurs at the β face of the eudesm-3-ene. In the case of eudesm-4(15)-enes, a β epoxide and other minor products were reported (4).

The configurations of natural α and β epoxides have been assigned only from a consideration of chemical shifts and coupling constants (5).

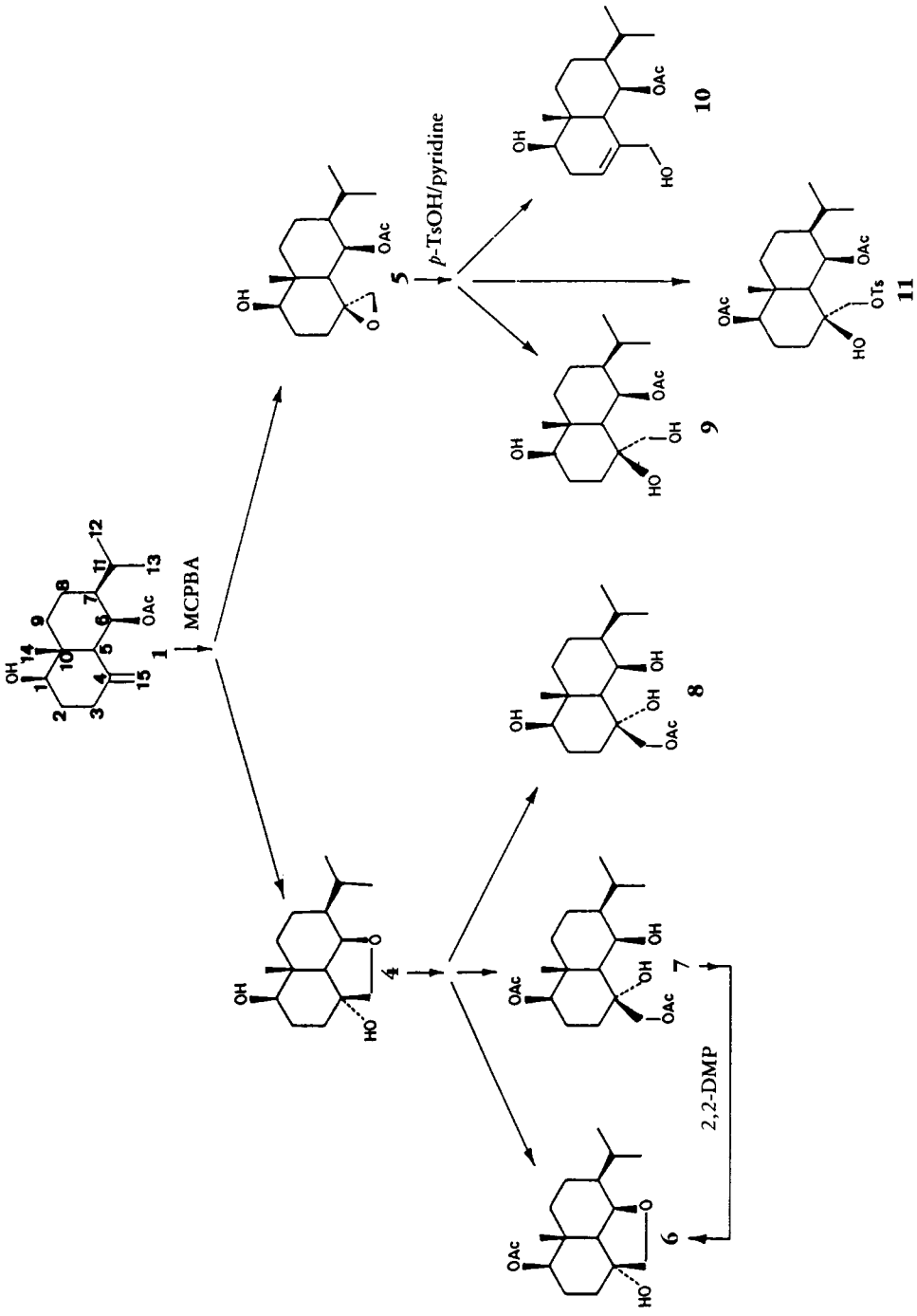
Rearrangements of 3α,4α-epoxyeudesmanes have been reported (6) to give, almost quantitatively, 3α-hydroxyeudesm-4(15)-ene systems. The rearrangement of 4α,5α-epoxides by HCl media yielded 4β-chloro-5α-hydroxyeudesmane and 5α-hydroxy-4(15)-eudesmene (minor) and the 2,4-diene (major product) after treatment with BF_3-etherate (7). Where the starting epoxide had a carbonyl group at C-1, formation of dienic compounds was observed.

In this work we studied the stereochemistry of epoxidation of 6β-acetoxyeudesmenes with unsaturation at the 4(15)-, 3-, and 4-positions (structures **1**, **2**, and **3**, respectively) and the products obtained from the epoxides by treatment in mild acid media.

RESULTS AND DISCUSSION

The epoxidation of 1β-hydroxy-6β-acetoxyeudesm-4(15)-ene [**1**] with *m*-chloroperbenzoic acid (MCPBA) in order to obtain a carbonyl group on C-4 was previously reported (4). Reinvestigation of this epoxidation process led to the isolation of a new product **4** and the epoxide **5** identical with that previously reported (4). The ^{1}H-nmr and ir spectra of **4** showed the absence of an acetoxyl group. Moreover, signals at δ 4.29 (false triplet, $J = 3.5$ Hz) attributable to H-6, a broad multiplet at δ 3.28 ($W_{1/2} = 20$ Hz) attributable to H-1, and an AB system with doublets centered at δ 3.83 and 3.40 ($J = 7$ Hz) were observed. The chemical shift of this AB system suggested the presence of a single oxymethylenic group, and the small value of its geminal coupling constant ($J = 7$ Hz) was compatible with a tetrahydrofuran system. The polarity (tlc) of **4** is lower than the polarity of epoxide **5**, which excluded a 1,6,15 trihydroxy structure for **4**.

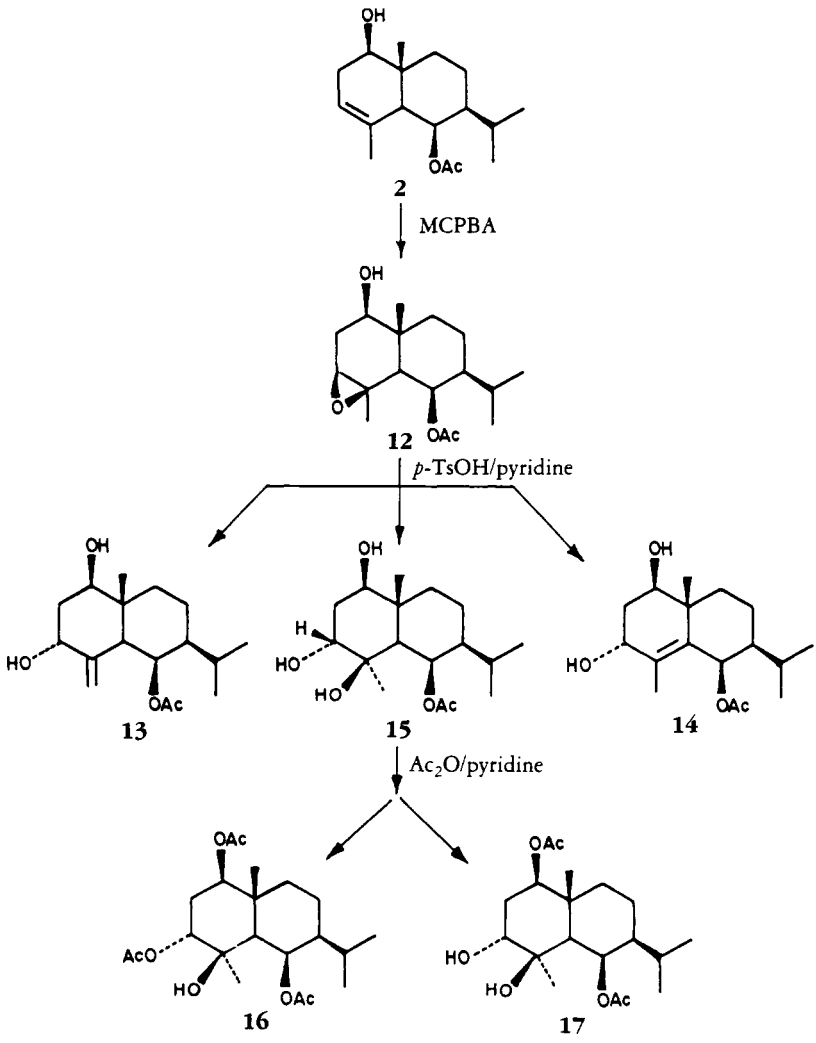
Mild acetylation of **4** gave three products, **6**, **7**, and **8**. The ir spectrum of **6** had bands characteristic of hydroxyl and acetoxyl groups. Its ^{1}H-nmr spectrum showed only one acetoxyl group (at C-1), which excludes the presence of a free hydroxyl group at C-15 in **4**. The ^{13}C-nmr spectrum of **6** indicated the presence of four oxygenated carbons (a primary one at δ 73.84, two secondaries at δ 79.09 and 67.07, and a tertiary one at δ 79.83), which confirmed the proposed structures for **4** and **6**.


MCPBA
p-TsOH/pyridine
2,2-DMP

Product **7** (also obtained by acetylation of **4**) is a diacetate (^{1}H nmr) with acetoxyl groups at C-1 and C-15 and a free hydroxyl group at C-6. In this case the ring was opened, and the two accessible positions C-1 and C-15 were then acetylated. The same configuration at C-4 is assigned for **7** as for **4** and **6**. Treatment of **7** with 2,2-dimethoxypropane and *p*-TsOH/pyridine gave **6**. Based on the structures proposed for **4**, **6**, and **7**, we propose the structure **8** for the product also obtained from acetylation of **4**.

NOe difference experiments performed on products **6**, **7**, and **8**, showed, in the case of **6**, a positive nOe effect between H-6 and the C-15 *cis* proton. In the case of **7** and **8**, the nOe effect between H-6 and the C-15 protons was insignificant (both of equal intensity). Also, each of the products **6**, **7**, and **8** showed an nOe effect between the methyl group at C-14 and the protons at C-15.

As indicated above, product **5** (56%) was isolated from epoxidation of **1**. In accordance with the structure of **4**, product **5** must be the 4β,15-epoxy derivative identical with that previously described (4). In this work we have confirmed the configuration at C-4 of **5** by means of nOe difference experiments. Irradiation at H-6 produced a large positive nOe effect (10%) on one of the C-15 protons (δ 3.16) and a weak one on the other (δ 2.20). Irradiation at δ 3.16 produced positive nOe effects on H-6 and on the



geminal proton at C-15. Irradiation at δ 2.20 produced a positive nOe effect on its geminal proton and a negative nOe on H-6, which confirms the configuration at C-4.

Treatment of **5** with *p*-TsOH/pyridine leads to two unstable products **9** and **10** and one stable product **11**. From the ^{1}H-nmr spectrum of **9** one may deduce that this product is a glycol that resulted from the opening of the epoxy group with the same configuration at C-4 as product **5**.

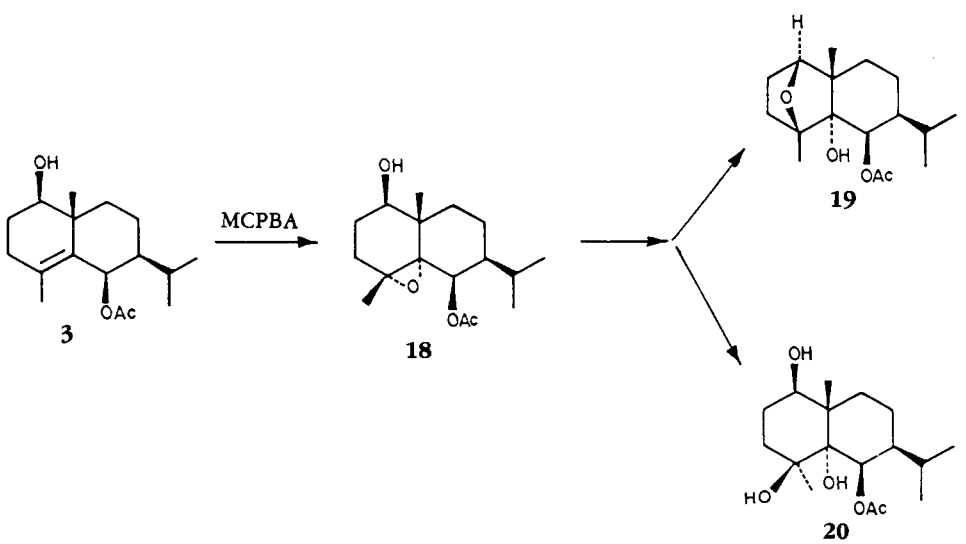
In the same way, the ^{1}H-nmr spectrum of **10** indicates that this product arose from rearrangement of the epoxide with elimination of the α proton at C-3 or resulted from dehydration of **9**. Product **11** may arise from the opening of epoxy compound **5** in acidic medium by attack of the tosylate group.

The configuration of 4-hydroxyeudesmanes has always been disputed (3, 8–10). In recent work products **12** and **13** have been published with the same configuration at C-4 as **7** and **8** (and opposite to **9** and **11**). These structures of **12** and **13** were determined exclusively by the study of their ^{1}H-nmr chemical shifts (10).

Epoxidation of **2** with MCPBA gave the β epoxide in good yield. A β epoxidation has previously been described for a substrate similar to **2** (3). Epoxidations at the α face were always justified by assuming association of the peracid with oxygens located axially at C-1 and also taking into account that rearrangement of the resulting epoxides with BF_3 leads to a 3α-hydroxyeudesm-4(15)-ene (1,6).

In this work we have also obtained 3α-hydroxy derivatives by rearrangement of the epoxide **12**, but we think that epoxidation occurs at the β face on the basis of our nOe difference experiments. Thus, irradiation of **12** at δ 5.60 (H-6) gives a high nOe effect on H-5 (δ 1.60) and on the methyl group at C-15 (δ 1.18). Similarly, irradiation of the C-15 methyl group produces a positive nOe effect on H-6 (δ 5.60) and H-3 (δ 2.90) but not on the C-14 methyl group (δ 0.91). In addition, irradiation of the C-14 methyl group does not produce an nOe on protons at C-3 and C-5. These data allow us to assign a 3β,4β configuration to epoxide **12** in agreement with Bohlmann *et al.* (3).

Treatment of **12** with *p*-TsOH/pyridine gave products **13** (44.4%), **14** (26.7%), and **15** (28.9%). Product **13** had an ^{1}H-nmr spectrum for which, in addition to the H-6 proton (δ 5.58, bs), two signals of an exocyclic methylene group (δ 5.03, bs and 4.83, d, $J = 2$ Hz, one H each), a signal of an equatorial proton (δ 4.32, dd, $J_1 = J_2 = 2$ Hz) geminal to an allylic hydroxyl group, and the H-1 proton considerably deshielded (δ 3.80, dd, $J_1 = 11$, $J_2 = 5$ Hz) can be seen. ^{13}C-nmr data supports the structure pro-



posed for **13**. Product **14** is very similar to **13** having an α hydroxyl group at C-3 and a Δ^4 double bond. The structures of **13** and **14** appear at first sight to support the α configuration for epoxide **12**. Nevertheless, in addition to the evidence for the structure of **12**, the structure of another product **15** isolated from this reaction may clarify the chemical pathway for formation of **13**, **14**, and **15**. Product **15** showed signals attributable to two methyl singlets (δ 1.44 and 1.26, 3H each) and two signals possibly due to the protons of C-1 and C-3, both geminal to hydroxyl groups and with coupling constants similar to those observed for a similar proton in the case of product **13**. The ^{13}C-nmr spectrum of **15** also indicates an hydroxyl group at C-4 (δ 74.39).

Treatment of **15** with 2,2-dimethoxypropane did not yield the acetonide derivative but gave **13** and **14**, which proved that all three products had the same configuration at C-3. The inability to form the acetonide strongly suggests the β disposition of the hydroxyl group at C-4, and this configuration was proved by H^1 nOe difference experiments of product **16**, a derivative of **15**.

Mild acetylation of **15** gave mainly the triacetate **16** as well as a diacetate **17** with the axial hydroxyl group at C-3 still present. Irradiation on H-6 of product **16** produced a positive nOe on H-5 (δ 1.42) and the C-15 methyl group (δ 1.38) and does not affect the C-14 methyl group. Irradiation at very low power and for a long time on the C-15 methyl group produced a strong nOe on H-6 (15%) and weaker but significant enhancement on H-3 (7%), possibly because of their relative proximity due to the almost equatorial disposition for both groups at C-5 and C-4. Irradiation under the same conditions on the C-14 methyl group (δ 1.35) gave no nOe with the above-mentioned protons.

In order to confirm the nOe's relative to the C-4 configuration, nOe difference experiments have been done on 1β,4β-dihydroxy-6β-acetoxyeudesmane and 1β,4α-dihydroxy-6β-acetoxyeudesmane (4,11) verifying that only the α methyl group at C-14 gives dipolar coupling with H-6. This fact confirms the proposed structure for product **15**.

Products **13** and **14**, thus, seem to arise by dehydration of the tertiary alcohol of **15** and not as direct rearrangement products from epoxide **12**. Product **15** comes from the opening of the oxirane ring of **12** at C-3 with inversion in the configuration of this carbon.

Epoxidation of the eudesm-4-ene **3** occurs by the α face as expected. NOe difference experiments are inconclusive; the study of molecular models indicates that nOe's between H-6 and the C-15 methyl group are possible for the α epoxide as well as for the β epoxide.

Treatment of **18** with *p*-TsOH/pyridine gave two products, **19** and **20**, of very different polarity. The less polar one, **19**, presented a substantial change in its nmr coupling, with H-1 now appearing as a sharp multiplet at δ 3.31 ($W_{1/2}$ = 10 Hz). As it has two methyl singlets it must be oxygenated at C-4, so compound **19** is the result of the opening of the 4α,5α-epoxide **18** by intramolecular attack of the hydroxyl group at C-1, after protonation of the epoxy group. We have observed that product **19** arises spontaneously, but slowly, from **18**.

The more polar product, **20**, obtained from **18** had oxygenated functions at C-1, C-4, C-5, and C-6, as can be proved from its ^{1}H- and ^{13}C-nmr spectra. Treatment of **20** with 2,2-dimethoxypropane gave epoxide **18** but not a cyclic acetonide, which indicated that the hydroxyl groups at C-4 and C-5 are *trans*. The configuration of C-4 has been deduced by means of nOe difference experiments. A positive nOe between H-6 and the C-15 methyl group was observed, which indicated that both groups are *cis*.

Product **20** must, therefore, be considered to be formed from the opening of the 4α,5α-epoxide **18** with inversion at C-4, yielding a 4β,5α-dihydroxy system.

This paper demonstrates the value of nOe difference experiments for the determination of configuration at C-4 in eudesmanes with complicated stereochemical problems.

EXPERIMENTAL

Mps were determined in a Kofler apparatus and are uncorrected. ^{1}H-*nmr spectra were measured at* 80 MHz and 300 MHz ($CDCl_3$ solution with TMS as internal standard). ^{13}C-nmr spectra were determined at 20.13 MHz (Bruker WP80SY) and at 75.74 MHz (Bruker AM300) also in $CDCl_3$ (which also provided the lock signal) with TMS added as internal reference. Assignments were made with the aid of distortionless enhancement by polarization transfer (DEPT) using a "flip angle" of 135°. NOe difference experiments were carried out at 300 MHz in a Bruker AM300 spectrometer with an irradiation time for nOe generation of 4 sec and a relaxation delay of 8 sec. Ir spectra were recorded in a Perkin-Elmer 983G spectrophotometer. The optical rotations were measured on a Perkin-Elmer 240 polarimeter. Mass spectra were carried out on a Hewlett-Packard 5988-A spectrometer. Si gel Merck 7729 (less than 0.08 mm) and Scharlau 60 were used for flash chromatography. The eluents used were CH_2Cl_2 and CH_2Cl_2 containing increasing amounts of Me_2CO.

GENERAL EPOXIDATION PROCEDURE.—Product was dissolved in CH_2Cl_2, and the appropriate amount of MCPBA was added with magnetic stirring. The course of reaction was followed by tlc, and, when complete, an aqueous solution of $FeSO_4$ was added to destroy excess of MCPBA, then washed with saturated $NaHCO_3$ and finally with H_2O. The organic solution was dried over anhydrous $MgSO_4$ and filtered, and the solvent evaporated under vacuum.

REARRANGEMENT WITH *p*-TsOH/PYRIDINE.—Product dissolved in $CHCl_3$ was treated with catalytic amounts of *p*-TsOH/pyridine under magnetic stirring at ambient temperature. Reaction was monitored by tlc. When finished, it was dried under vacuum, redissolved in CH_2Cl_2, washed with H_2O to remove *p*-TsOH/pyridine and dried over anhydrous $MgSO_4$, and the solvent evaporated.

REARRANGEMENT WITH BF_3-ETHERATE.—Product was dissolved in dry $CHCl_3$ and stirred with a magnetic stirrer in an ice bath. Five drops of BF_3 were then added. The reaction was completed in 5 min, and then washed with diluted solution of $NaHCO_3$, dried over anhydrous $MgSO_4$, and filtered, and the solvent evaporated at reduced pressure.

TREATMENT WITH 2,2-DIMETHOXYPROPANE.—Product was dissolved in 2,2-dimethoxypropane with a few drops of Me_2CO, and a catalytic amount of *p*-TsOH/pyridine was added. After refluxing 2 h, the mixture was evaporated and redissolved in CH_2Cl_2, washed with H_2O to remove *p*-TsOH/pyridine and dried over anhydrous $MgSO_4$.

GENERAL ACETYLATION PROCEDURE.—Product was dissolved in a mixture of Ac_2O-pyridine (1:2) and stirred at 0° for 2 h. The reaction product was poured into cold H_2O and extracted with CH_2Cl_2, washed with diluted HCl and $NaHCO_3$ solution. The CH_2Cl_2 layer was dried over $MgSO_4$ and evaporated at reduced pressure. For some products acetylation was done at high temperature. The general procedure was the same; *the reaction mixture was refluxed for 1 h instead of keeping it at* 0°.

FORMATION AND REARRANGEMENT OF THE EPOXIDE OF 1β-HYDROXY-6β-ACETOXYEUDESM-4(15)-ENE [**1**].—Product **1** (300 mg) was treated with MCPBA as in the general procedure. After cc, the following products were obtained: 1β,4α-dihydroxy-6β,15-epoxyeudesmane [**4**], 80 mg and 1β-hydroxy-4β,15-epoxy-6β-acetoxyeudesmane [**5**], 100 mg.

1β,4α-dihydroxy-6β,15-epoxyeudesmane [**4**].—^{1}H nmr (80 MHz) δ 4.29 (1H, dd, $J_1 = J_2 = 3$ Hz, H-6), 3.83 and 3.40 (1H each, AB system, $J = 7$ Hz, 2H-15), 3.28 (1H, m, $W_{1/2} = 20$ Hz, H-1), 1.54 (3H, s, 14-Me), 0.96 and 0.93 (3H each, d, $J = 7$ Hz, 12-Me and 13-Me); ms *m/z* (rel. int.) $[M]^+$ 254 (34), 236 (100), 221 (9), 193 (19), 179 (7), 165 (58), 152 (37), 151 (43), 147 (41), 138 (7), 135 (19), 133 (24), 123 (69), 121 (29), 120 (22), 119 (29), 117 (10), 108 (27), 107 (34), 106 (34), 105 (49).

1β-hydroxy-4β,15-epoxy-6β-acetoxyeudesmane [**5**].—Colorless gum, $[\alpha]^{20}D$ +1.93° ($CHCl_3$, $c = 1$); ir ν max (film) cm^{-1} 3460, 2890, 2850, 1720, 1450, 1370, 1250, 1210, 1180, 1140, 1005, 970; ^{1}H nmr (300 MHz) δ 5.25 (1H, bs, H-6), 3.30 (1H, dd, $J_1 = 12$, $J_2 = 4$ Hz, H-1), 3.16 and 3.20 (1H each, AB system, $J = 4$ Hz, 2H-15), 2.05 (3H, s, AcO), 1.17 (3H, s, 14-Me), 0.92 and 0.87 (3H each, d, $J = 7$ Hz, 12-Me and 13-Me); ^{13}C nmr see Table 1. Ms *m/z* (rel. int.) $[M - 15]^+$ 201 (1), 266 (4), 253 (71), 248 (8), 237 (34), 236 (36), 224 (52), 221 (27), 209 (32), 206 (47), 193 (55), 188 (34), 180 (56), 173 (23), 163 (42), 145 (59), 137 (38), 123 (56), 109 (44), 107 (62), 105 (59).

ACETYLATION OF **4**.—Product **4** (80 mg) was treated as in general procedure. After cc the following products were isolated in order of elution: 1β-acetoxy-4α-hydroxy-6β,15-epoxyeudesmane [**6**], 11 mg,

1β,15-diacetoxy-4α,6β-dihydroxyeudesmane [**7**], 36 mg, and 1β,4α,6β-trihydroxy-15-acetoxyeudesmane [**8**], 32 mg.

1β-acetoxy-4α-hydroxy-6β,15-epoxyeudesmane [**6**].—Colorless gum; $[\alpha]^{20}D$ +0.20° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 3750, 3500, 2910, 1730, 1460, 1370, 1290, 1180, 1140, 1120, 990; ^1H nmr (300 MHz) δ 4.55 (1H, dd, J_1 = 10, J_2 = 4 Hz, H-1), 4.29 (1H, bt, J = 4 Hz, H-6), 3.83 and 3.39 (1H each, AB system, J = 7 Hz, 2H-15), 2.05 (3H, s, AcO), 1.55 (3H, s, 14-Me), 0.97 and 0.92 (3H each, d, J = 7 Hz, 12-Me and 13-Me); ^{13}C nmr see Table 1.

1β,15-diacetoxy-4α,6β-dihydroxyeudesmane [**7**].—Colorless gum; $[\alpha]^{20}D$ +16.8° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 3480, 2900, 2860, 1730, 1370, 1260, 1190, 1000, 965; ^1H nmr (300 MHz) δ 4.45 (1H, dd, J_1 = 11, J_2 = 4 Hz, H-1), 4.35 (1H, bt, J = 4 Hz, H-6), 4.15 and 3.92 (1H each, AB system, J = 12 Hz, 2H-15), 2.06 and 2.04 (3H each, s, 2AcO), 1.40 (3H, s, 14-Me), 0.94 (6H, d, J = 6 Hz, 12-Me and 13-Me); ms *m/z* (rel. int.) $[M - AcOCH_2]^+$ 283 (49), 265 (28), 223 (11), 205 (100), 187 (37), 177 (7), 163 (11), 149 (23), 145 (22), 131 (11), 121 (13), 109 (20), 107 (22), 105 (21). *Anal.* calcd for $C_{19}H_{32}O_6$: C 64.05, H 8.98, O 26.96. Found: C 63.71, H 8.90, O 27.39.

1β,4α,6β-trihydroxy-15-acetoxyeudesmane [**8**].—Colorless gum, $[\alpha]^{20}D$ +11.8° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 3470, 2900, 2860, 1735, 1370, 1190, 995; ^1H nmr (300 MHz) δ 4.38 (1H, bs, H-6), 4.15 and 3.95 (1H each, AB system, J = 12 Hz, 2H-15), 3.20 (1H, dd, J_1 = 11, J_2 = 4 Hz, H-1), 2.05 (3H, s, AcO), 1.34 (3H, s, 14-Me), 0.96 (6H, d, J = 6 Hz, 12-Me and 13-Me); ms *m/z* (rel. int.) $[M-AcOCH_2]^+$ 241 (76), 223 (100), 205 (50), 187 (21), 177 (7), 167 (9), 163 (10), 149 (19), 145 (27), 135 (9), 123 (15), 121 (17), 119 (9), 109 (24), 107 (24), 105 (13). *Anal.* calcd for $C_{17}H_{30}O_5$: C 64.95, H 9.55, O 25.47. Found: C 64.39, H 9.62, O 25.62.

TREATMENT OF **7** WITH 2,2-DIMETHOXYPROPANE.—Product **7** (30 mg) was treated with 2,2-dimethoxypropane as indicated above. After cc, only product **6** was isolated.

TREATMENT OF **5** WITH *p*-TsOH/PYRIDINE.—Product **5** (50 mg) was processed as in general procedure, yielding after cc the products 1β,4β,15-trihydroxy-6β-acetoxyeudesmane [**9**] (18 mg), 1β,15-dihydroxy-6β-acetoxyeudesm-3-ene [**10**] (20 mg), 1β,6β-diacetoxy-4β-hydroxy-15-tosyloxyeudesmane [**11**] (6 mg).

1β,4β,15-trihydroxy-6β-acetoxyeudesmane [**9**].—Colorless gum; ^1H nmr (80 MHz) δ 6.00 (1H, d, J = 2 Hz, H-6), 4.63 and 3.50 (1H each, AB system, J = 12 Hz, 2H-15), 3.40 (1H, dd, J_1 = 11, J_2 = 7 Hz, H-1) 2.03 (3H, s, AcO), 1.12 (3H, s, 14-Me), 0.96 and 0.92 (3H each, d, J = 6 Hz, 12-Me and 13-Me).

1β,15-dihydroxy-6β-acetoxyeudesm-3-ene [**10**].—Colorless gum; ^1H nmr (80 MHz) δ 5.77 (1H, bs, H-6), 5.66 (1H, m, $W_{1/2}$ = 12 Hz, H-3), 4.20 and 3.95 (1H each, AB system, J = 12 Hz, 2H-15), 3.50 (1H, dd, J_1 = 11, J_2 = 5 Hz, H-1), 2.03 (3H, s, AcO), 0.96 (3H, s, 14-Me), 0.97 and 0.93 (3H each, d, J = 6 Hz, 12-Me and 13-Me).

1β,6β-diacetoxy-4β-hydroxy-15-tosyloxyeudesmane [**11**].—Colorless gum; $[\alpha]^{20}D$ +36° ($CHCl_3$, c = 0.5); ir ν max (film) cm^{-1} 3496, 2932, 1739, 1608, 1453, 1367, 1242, 1177, 1098, 1032, 930, 840; ^1H nmr (80 MHz) δ 7.80 and 7.32 (2H each, A_2B_2 system, J = 8 Hz, 4H-Ts group), 5.35 (1H, bs, H-6), 4.40 (1H, m, $W_{1/2}$ = 18 Hz, H-1), 4.30 and 3.90 (1H each, AB system, J = 10 Hz, 2H-15), 2.43 and 1.33 (3H each, s, Ts and 14-Me), 2.02 and 1.95 (3H each, s, 2AcO), 0.82 and 0.80 (3H each, d, J = 6 Hz, 12-Me and 13-Me).

EPOXIDATION OF 1β-HYDROXY-6β-ACETOXYEUDESM-3-ENE [**2**].—Product **2** (250 mg) was treated with MCPBA as described above to give 1β-hydroxy-6β-acetoxy-3-epoxyeudesmane [**12**] (200 mg).

1β-hydroxy-6β-acetoxy-3-epoxyeudesmane [**12**].—Colorless gum; $[\alpha]^{20}D$ +34.5° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 3460, 1745, 1250, 1230; ^1H nmr (80 MHz) δ 5.65 (1H, bs, H-6), 3.28 (1H, dd, J_1 = 11, J_2 = 6 Hz, H-1), 2.97 (1H, bd, J = 3 Hz, H-3), 2.07 (3H, s, AcO), 1.25 and 0.99 (3H each, s, 14-Me and 15-Me), 1.00 and 0.85 (3H each, d, J = 6 Hz, 12-Me and 13-Me); ^{13}C nmr see Table 1; ms *m/z* (rel. int.) $[M]^+$ 296 (8), 236 (15), 221 (8), 218 (5), 192 (41), 165 (19), 149 (10), 137 (67), 121 (23), 110 (10), 109 (16), 107 (14), 105 (8). *Anal.* calcd for $C_{17}H_{28}O_4$: C 68.92, H 9.46, O 21.62. Found: C 68.63, H 9.97, O 21.40.

TREATMENT OF **12** WITH *p*-TsOH/PYRIDINE.—Product **12** (80 mg) was treated with *p*-TsOH/pyridine as described earlier. After cc, 1β,3α-dihydroxy-6β-acetoxyeudesm-4(15)-ene [**13**] (20 mg), 1β,3α-dihydroxy-6β-acetoxyeudesm-4-ene [**14**] (12 mg), and 1β,3α,4β-trihydroxy-6β-acetoxyeudesmane [**15**] (13 mg) were isolated.

1β,3α-dihydroxy-6β-acetoxyeudesm-4(15)-ene [**13**].—Colorless gum; $[\alpha]^{20}D$ +19.8° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 2900, 2840, 1725, 1370, 1000; ^1H nmr (80 MHz) δ 5.58 (1H, bs, H-6), 5.03 (1H, bs, 1H-15), 4.83 (1H, d, J = 2 Hz, 1H-15), 4.32 (1H, t, J = 2.5 Hz, H-3), 3.80 (1H, dd, J_1 = 11, J_2 = 5 Hz, H-1), 2.42 (1H, bs, H-5), 2.05 (3H, s, AcO), 0.94 (3H, s, 14-Me), 1.00 and 0.90 (3H each, d, J = 6 Hz, 12-Me and 13-Me); ^{13}C nmr see Table 1; ms *m/z* (rel. int.) $[M]^+$ 296 (2), 236 (27), 221 (20), 218 (25), 203 (12), 193 (79), 192 (100), 175 (42), 157 (13), 149 (30), 147 (29), 133 (24), 121 (41), 109 (38), 107 (44), 105 (45).

1β,3α,dihydroxy-6β-acetoxyeudesm-4-ene [**14**].—Colorless gum; $[\alpha]^{20}D$ +95° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 2900, 2870, 1725, 1370, 995; ^1H nmr (80 MHz) δ 5.95 (1H, d, J = 2 Hz, H-6), 4.07 (1H, bt, J = 3 Hz, H-3), 3.69 (1H, dd, J_1 = 9, J_2 = 6 Hz, H-1), 2.00 (3H, s, AcO), 1.98 and 1.07 (3H each, s, 15-Me and 14-Me), 0.93 (6H, d, J = 6 Hz, 12-Me and 13-Me); ^{13}C nmr see Table 1; ms *m/z* (rel. int.) $[M\text{-AcOH}]^+$ 236 (18), 221 (5), 218 (10), 194 (14), 193 (100), 175 (26), 165 (7), 161 (4), 157 (4), 149 (24), 147 (12), 137 (5), 135 (6), 133 (7), 131 (8), 123 (7), 121 (15), 109 (11), 107 (9), 105 (11).

1β,3α,4β-trihydroxy-6β-acetoxyeudesmane [**15**].—Colorless gum; $[\alpha]^{20}D$ +42° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 2890, 2855, 1725, 1450, 1370, 1190, 1140, 1000; ^1H nmr (80 MHz) δ 5.65 (1H, bs, H-6), 3.62 (1H, dd, J_1 = 11, J_2 = 4 Hz, H-1), 3.55 (1H, m, $W_{1/2}$ = 6 Hz, H-3), 2.00 (3H, s, Aco), 1.44 and 1.26 (3H each, s, 14-Me and 15-Me), 0.93 and 0.90 (3H each, d, J = 6 Hz, 12-Me and 13-Me); ^{13}C nmr see Table 1.

ACETYLATION OF **15**.—Product **15** (13 mg) was treated with Ac_2O/pyridine as described previously to give 1β,3α,6β-triacetoxy-4β-hydroxyeudesmane [**16**] (10 mg) and 1β,6β-diacetoxy-3α,4β-dihydroxyeudesmane [**17**] (1.5 mg).

1β,3α,6β-triacetoxy-4β-hydroxyeudesmane [**16**].—Colorless gum; $[\alpha]^{20}D$ +0.1° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 3492, 2929, 2857, 1734, 1371, 1242, 1040; ^1H nmr (300 MHz) δ 5.62 (1H, bs, H-6), 4.85 (1H, dd, J_1 = 12, J_2 = 4 Hz, H-1), 4.75 (1H, m, $W_{1/2}$ = 6 Hz, H-3), 2.08 (3H, s, AcO), 2.03 (6H, s, 2AcO), 1.35 and 1.25 (3H each, s, 14-Me and 15-Me), 0.90 and 0.86 (3H each, d, J = 6 Hz, 12-Me and 13-Me); ms *m/z* (rel. int.) $[M - 2AcOH]^+$ 278 (18), 236 (18), 218 (26), 203 (10), 201 (46), 175 (14), 159 (35), 149 (12), 148 (10), 147 (10), 151 (56), 137 (60), 134 (17), 123 (12), 121 (13), 119 (11), 109 (15), 107 (19), 105 (17). *Anal.* calcd for $C_{21}H_{34}O_7$: C 63.31, H 8.54, O 28.14. Found: C 62.92, H 8.89, O 28.19.

1β,6β-diacetoxy-3α,4β-dihydroxyeudesmane [**17**].—Colorless gum; ^1H nmr (80 MHz) δ 5.63 (1H, bs, H-6), 4.92 (1H, dd, J_1 = 11, J_2 = 4 Hz, H-1), 3.38 (1H, bt, J = 3 Hz, H-3), 2.05 (6H, s, 2AcO), 1.47 and 1.35 (3H each, s, 14-Me and 15-Me), 0.95 and 0.90 (3H each, d, J = 6 Hz, 12-Me and 13-Me).

EPOXIDATION OF 1β-HYDROXY-6β-ACETOXYEUDESM-4-ENE [**3**].—Product **3** (250 mg) was treated with MCPBA as described above to give 1β-hydroxy-4α,5α-epoxy-6β-acetoxyeudesmane [**18**] (210 mg).

1β-hydroxy-4α,5α-epoxy-6β-acetoxyeudesmane [**18**].—Colorless gum; $[\alpha]^{20}D$ −16.2° ($CHCl_3$, c = 1); ir ν max (film) cm^{-1} 2900, 2850, 1730, 1455, 1370, 1120, 1000, 987; ^1H nmr (300 MHz) δ 4.92 (1H, bs, H-6), 3.77 (1H, dd, J_1 = 11, J_2 = 6 Hz, H-1), 2.09 (3H, s, AcO), 1.35 and 1.10 (3H each, s, 15-Me and 14-Me), 0.91 (6H, d, J = 6 Hz, 12-Me and 13-Me); ^{13}C nmr see Table 1; ms *m/z* (rel. int.) $[M - AcOH]^+$ 236 (3), 227 (1), 221 (1), 193 (86), 183 (2), 179 (7), 175 (5), 154 (30), 151 (7), 135 (6), 133 (5), 131 (2), 123 (7), 121 (5), 111 (26), 101 (100).

REARRANGEMENT OF **18**.—Treatment of **18** with *p*-TsOH/pyridine in the usual manner gave 1β,4β-epoxy-5α-hydroxy-6β-acetoxyeudesmane [**19**] (6 mg) and 1β,4β,5α-trihydroxy-6β-acetoxyeudesmane [**20**] (20 mg). Rearrangement with BF_3 etherate gave the same products.

1β,4β-epoxy-5α-hydroxy-6β-acetoxyeudesmane [**19**].—Colorless gum; $[\alpha]^{20}D$ +1° ($CHCl_3$, c = 0.5); ir ν max (film) cm^{-1} 3471, 2930, 1717, 1453, 1372, 1254; ^1H nmr (80 MHz) δ 5.50 (1H, d, J = 3 Hz, H-6), 3.31 (1H, m, $W_{1/2}$ = 10 Hz, H-1), 2.10 (3H, s, AcO), 1.45 and 1.30 (3H each, s, 15-Me and 14-Me), 0.92 and 0.89 (3H each, d, J = 6 Hz, 12-Me and 13-Me).

1β,4β,5α-trihydroxy-6β-acetoxyeudesmane [**20**].—Mp 62–64°, $[\alpha]^{20}D$ +29.0° ($CHCl_3$, c = 1); ir ν max (KBr) cm^{-1} 3497, 2957, 1728, 1475, 1453, 1378, 1256, 1077, 1039, 1011, 992, 971, 932; ^1H nmr (300 MHz) δ 5.22 (1H, bs, H-6), 3.75 (1H, dd, J_1 = 11, J_2 = 4 Hz, H-1), 2.04 (3H, s, AcO), 1.40 and 1.30 (3H each, s, 15-Me and 14-Me), 0.90 and 0.87 (3H each, d, J = 6.5 Hz, 12-Me and 13-Me); ^{13}C nmr see Table 1; ms *m/z* (rel. int.) $[M - AcOH]^+$ 254 (13), 236 (8), 218 (4), 207 (4), 193 (28), 175 (13), 165 (6), 163 (5), 161 (6), 159 (6), 154 (11), 150 (13), 147 (13), 142 (35), 140 (27), 139 (44), 109 (50), 107 (41), 105 (27). *Anal.* calcd for $C_{17}H_{30}O_5$: C 64.96, H 9.55, O 25.47. Found: C 64.45, H 10.01, O 25.54.

TABLE 1. ^{13}C-nmr Chemical Shifts[a] of Compounds **5–7**, **12–15**, **18**, and **20**.

Carbon	Compound								
	5	**6**	**7**	**12**	**13**	**14**	**15**	**18**	**20**
1	79.46	79.10	82.36	75.07	75.01	73.71	75.56	72.99	73.43
2	27.75	29.39	36.56	30.56	37.23	38.44	34.11	28.70	27.27
3	33.96	37.47	26.23	61.19	74.37	71.04	74.89	24.96	33.45
4	58.26	79.84	74.07	57.91	147.72	—	74.39	64.46	76.19
5	49.11	46.29	50.56	51.36	46.42	—	47.65	69.94	75.74
6	68.70	67.07	70.16	71.20	71.23	70.94	71.26	72.99	72.54
7	46.55	45.77	51.64	49.96	50.23	48.62	49.78	45.69	43.18
8	20.52	21.54	23.18	19.95	20.45	20.32	20.57	20.31	21.14
9	37.61	24.36	41.52	35.62	37.23	36.05	39.70	33.88	37.59
10	40.11	36.90	40.08	37.38	40.63	39.67	39.70	37.42	42.43
11	28.32	28.75	31.52	28.41	28.34	29.15	29.80	28.70	28.85
12	21.17	21.22	24.32	21.43	21.47	20.88	21.39	20.59	20.75
13	20.32	20.90	24.32	20.23	21.47	20.88	20.97	21.12	21.32
14	13.04	17.21	19.08	13.03	12.16	17.23	14.09	13.90	13.53
15	47.65	73.84	71.18	—	112.24	16.87	26.18	21.30	25.30
CH_3-COO	—	22.46	—	22.03	21.85	21.32	21.39	21.30	—
Me-*C*OO	170.1	171.0	167.2	170.1	170.85	—	171.3	169.4	170.0

[a]The ^{13}C chemical shifts are given in ppm to TMS.

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