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Biogenetically Patterned Transformation of Eudesmanolide to Eremophilanolide. V.[1] Studies on Stereochemical Factors for Favorable Conversion of 5α,6α-Epoxy-eudesman-8β, 12-olide leading to Eremophilane-type Derivatives

Isao Kitagawa, Hirotaka Shibuya, and Hiromichi Fujioka

Faculty of Pharmaceutical Sciences, Osaka University[2]

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In continuing studies on the elucidation of essential factors for the favorable biogenetic-type angular methyl migration starting from 5α,6α-epoxy-eudesman-8β,12-olide (**1**) leading to several eremophilanolides, four related eudesmane-type 5,6-epoxides (**4**, **5**, **6**, **7**) have been prepared and treated under four different acid conditions. Based on the product analyses, it has been demonstrated that the following three factors seem to be important for the biogenetic-type 10-methyl migration of **1** giving eremophilane-type derivatives: i) the presence of 5α,6α-epoxide function, ii) the spatial interaction between 10-methyl and 4β-methyl which would bring about distortion of the ring A, and iii) the presence of *cis*-γ-lactone moiety attached to C-7 and C-8.

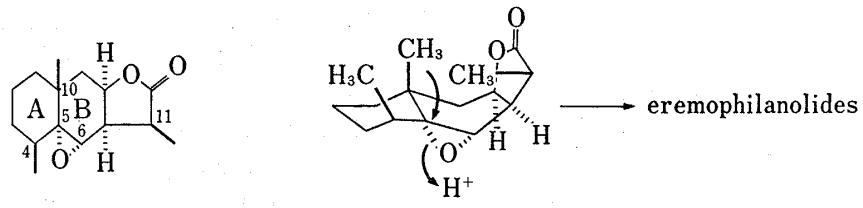
Keywords——biogenetic-type transformation; 5α,6α-epoxy-11βH-eudesman-8β,12-olide; 5α,6α-epoxy-4βH-eudesman-8β,12-olide; 8β-acetoxy-5α,6α-epoxy-eudesmane; 8β-acetoxy-5β,6β-epoxy-eudesmane; transformation under acid conditions; gas–liquid chromatography

During the course of studies on the biogenetic-type 1,2-shift of the angular methyl at C-10 of eudesmane-type sesquiterpene leading to eremophilane-type compounds, we have found that treatment of 5α,6α-epoxy-eudesman-8β,12-olide (**1**) with a formic acid–acetone (1:2) mixture under reflux furnishes five eremophilanolides in combined good yields.[3] We have also found that increase of the formic acid composition in the acidic medium (*e.g.* formic acid–acetone=2:1) results in formation of eremophilanolides in higher yields.[3b] Furthermore, in a recent study, we have successfully applied this biogenetic-type angular methyl migration to conversion of alantolactone (**2**) to several furanoeremophilane derivatives.[1]

As for the stereochemical reasons for the facile 1,2-shift of the angular methyl at C-10 in **1**, the following three factors would be presumably responsible: [1] the presence of 5α,6α-epoxide function, which selectively induces the carbonium cation formation at C-5 by opening of the oxirane ring on acid treatment, [2] the presence of methyls at C-4 and C-11, which causes considerable spatial interaction against the methyl at C-10 and would bring about distortion of the ring A, thus resulting in thermodynanic instability of **1**, and [3] the presence of *cis*-γ-lactone ring attached to C-7 and C-8, which would settle the boat-like conformation[4] of **1**, thus probably being favored for the methyl migration from C-10 (*cf.* **i**).

In order to examine the factor [1] among these, acid treatment of 4α,5α-epoxy-eudesman-8β,12-olide (**3**) was previously carried out and found to be no formation of eremophilane-type

1) Part IV: I. Kitagawa, H. Shibuya, and M. Kawai, *Chem. Pharm. Bull.* (Tokyo), **25**, 2638 (1977).
2) Location: *133–1, Yamada-kami, Suita, Osaka 565, Japan.*
3) *a*) I. Kitagawa, Y. Yamazoe, R. Takeda, and I. Yosioka, *Tetrahedron Lett.*, **1972**, 4843; *b*) I. Kitagawa, Y. Yamazoe, H. Shibuya, R. Takeda, H. Takeno, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **22**, 2662 (1974); *c*) I. Kitagawa, H. Shibuya, Y. Yamazoe, H. Takeno, and I. Yosioka, *Tetrahedron Lett.*, **1974**, 111; *d*) I. Kitagawa, H. Shibuya, H. Takeno, T. Nishino, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), **24**, 56 (1976).
4) M. Curie and G.A. Sim, *J. Chem. Soc. Perkin II*, **1973**, 400.



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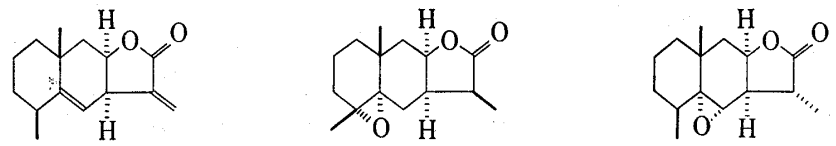

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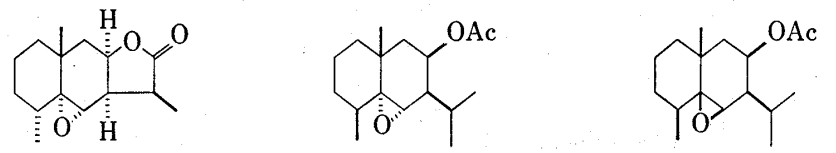


5 6 7

Chart 1

TABLE I. Stereochemical Features in **1**, **3**, **4**, **5**, **6**, and **7**

	Spatial interaction between 10–CH_3 and		Presence of *cis*-γ-lactone	Position of epoxide
	4–CH_3[a]	11–CH_3		
1	+	+	+	5α, 6α
3	−	+	+	4α, 5α
4	+	−	+	5α, 6α
5	−	+	+	5α, 6α
6	+	−	−	5α, 6α
7	+	−	−	5β, 6β

a) Each compound possessing the spatial interaction (marked with +) would simultaneously suffer the distortion of its ring A conformation.

compound in this case.[5] In continuing studies on the elucidation of essential factors for the favorable biogenetic-type methyl migration, we have prepared four eudesmane-type epoxides (**4**, **5**, **6**, and **7**) to examine their behavior for acid treatment under various conditions. The present paper deals with details of these product analyses, and, on these bases, comments on the important factors for the methyl migration. Stereochemical features in **1**, **3**, **4**, **5**, **6**, and **7**, which are noticed by Dreiding model examinations, are summarized in Table I.

Preparation of Three 5α,6α-Epoxides (4, 5, 6) and One 5β,6β-Epoxide (7)

Treatment of 5α,6α-epoxy-eudesman-8β,12-olide (**1**) with potassium carbonate in toluene under reflux furnished an equilibrated mixture of **1** and its 11α-methyl isomer (**4**) (the ratio of **1** and **4**=5: 1). The infrared (IR) spectrum of the minor isomer (**4**) shows absorption

5) I. Kitagawa, H. Takeno, H. Shibuya, and I. Yosioka, *Chem. Pharm. Bull.* (Tokyo), 23, 2686 (1975).

bands due to γ-lactone (1766 cm^{-1}) and epoxide (987 cm^{-1}), while the proton magnetic resonance (PMR) spectrum shows a broad singlet at δ 2.86 assignable to epoxidic 6-H. In the circular dichroism (CD) spectrum of **4**, a negative maximum at 216 nm ($[\theta]$ −1580) due to n→π^* transition of the lactone carbonyl is observed, thus the structure of 5α,6α-epoxy-11β-H-eudesman-8β,12-olide (**4**) having 11α-methyl being confirmed ($[\theta]_{218}$+720 for **1**).[5,6]

Isomerization of dihydroisoalantolactone (**8**)[7] by treatment with *p*-toluenesulfonic acid in acetic acid under reflux furnished a 5:1 mixture of **9** and **10**. The structure of the major (**9**) was already clarified in our previous report,[5] whereas the minor has been elucidated to be **10** on the following bases. The spectral properties of **10** are quite alike those of dihydroalantolactone (**11**).[7] The significant difference in the PMR spectra of **10** and **11** is that a signal due to an olefinic proton at C-6 is observed as a doublet of J=4 Hz in **11** (coupling only with 7α-H) while as a triplet of J= 3 Hz ($J_{4,6}=J_{6,7}$) in **10**. The fact is well explained by the structure **10** having a 4α-methyl function since 6-H and 4β-H (axial character) in **10** is anticipated to be in a long-range coupling. Oxidation of **10** with *m*-chloroperbenzoic acid furnished a single epoxide (**5**) which is assigned as the 5α,6α-epoxide of **10** as based on the preferential α-attack of the reagent. The spectral properties of **5** are also consistent with the assignment. The IR spectrum shows absorption bands of γ-lactone (1765 cm^{-1}) and epoxide (975 cm^{-1}), and the PMR spectrum exhibits a broad singlet of $W_{h/2}$=3 Hz at δ 3.11 assignable to 6-H, whose signal pattern is very similar to that in **1** (δ 2.85, $W_{h/2}$=3 Hz).[3]

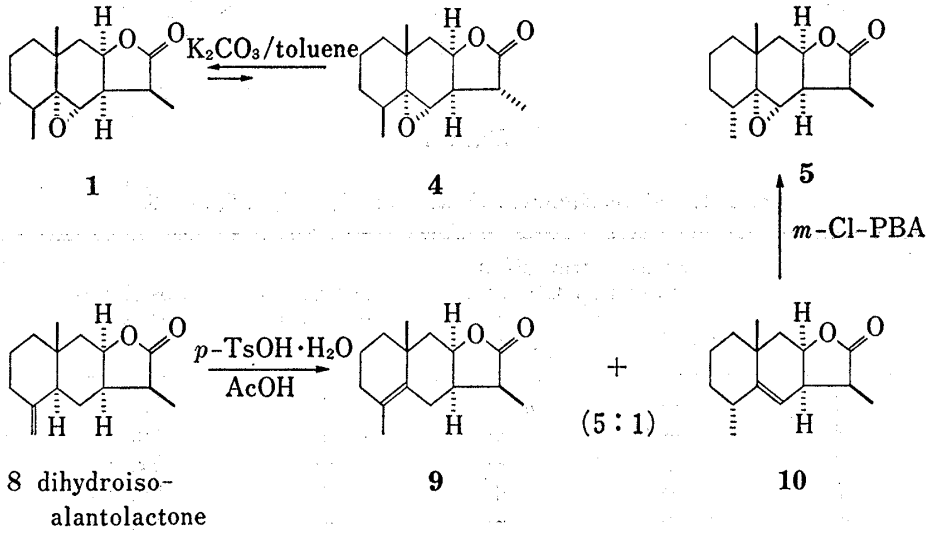


Chart 2

The pair of epoxides (**6, 7**) were synthesized as below. Lithium aluminum hydride reduction of dihydroalantolactone (**11**) gave a diol (**12**) which, on acetylation, was converted to a diacetate (**13**). Partial hydrolysis of **13** under carefully controlled conditions furnished a monoacetate (**14**), which was converted to a monoacetoxyl-mesylate (**15**). The structures of derivatives in the reaction sequence (**12, 13, 14**) have been substantiated by their spectral properties. Treatment of the mesylate (**15**) with excess sodium iodide afforded an iodo-derivative (**16**) which, on reduction with sodium borohydride in dimethyl sulfoxide (DMSO), was converted to a monoacetoxyl derivative (**17**). The structure of **17** has been corroborated by its spectral properties as given in the Experimental section. The overall yield from **11** to **17** was 62%. Finally, oxidation of **17** with *m*-chloroperbenzoic acid furnished two epoxides in a 3:1 ratio. Based on stereochemical considerations for the oxidation and PMR signals

6) G. Snatzke, H. Ripperger, C. Horstmann, and K. Schreiber, *Tetrahedron*, **22**, 3103 (1966).
7) *a*) K. Tsuda, K. Tanabe, I. Iwai, and K. Funakoshi, *J. Am. Chem. Soc.*, **79**, 5721 (1957); *b*) J.A. Marshall and N. Cohen, *J. Org. Chem.*, **29**, 3727 (1964).

assignable to the epoxidic proton (6-H) in both epoxides (br.s at δ 2.84 in the major epoxide; d of $J=$ 4 Hz at δ 2.93 in the minor), the major has been assigned as the 5α,6α-epoxide (**6**) and the minor as the 5β,6β-epoxide (**7**). The assignment has been further substantiated by the following derivation. Lithium aluminum hydride reduction of 5α,6α-epoxy-eudesman-8β,12-olide (**1**) primarily yielded an epoxy-diol (**18**). However, **18** was fairly labile and readily changeable to another unstable isomer, which has been presumably formulated as **18a**,[8] so that the epoxy-diol (**18**) was immediately converted to its monoacetate (**19**). On irradiation of a solution of the epoxy-monoacetate (**19**) in hexamethylphosphoric triamide (HMPA) and water[10] using a 30 W low pressure mercury lamp, was obtained a product, which, in turn, was acetylated to furnish an epoxy-acetate. The final product was found to be identical to the above-mentioned major epoxide **6**, thus the structures of **6** and **7** being confirmed.

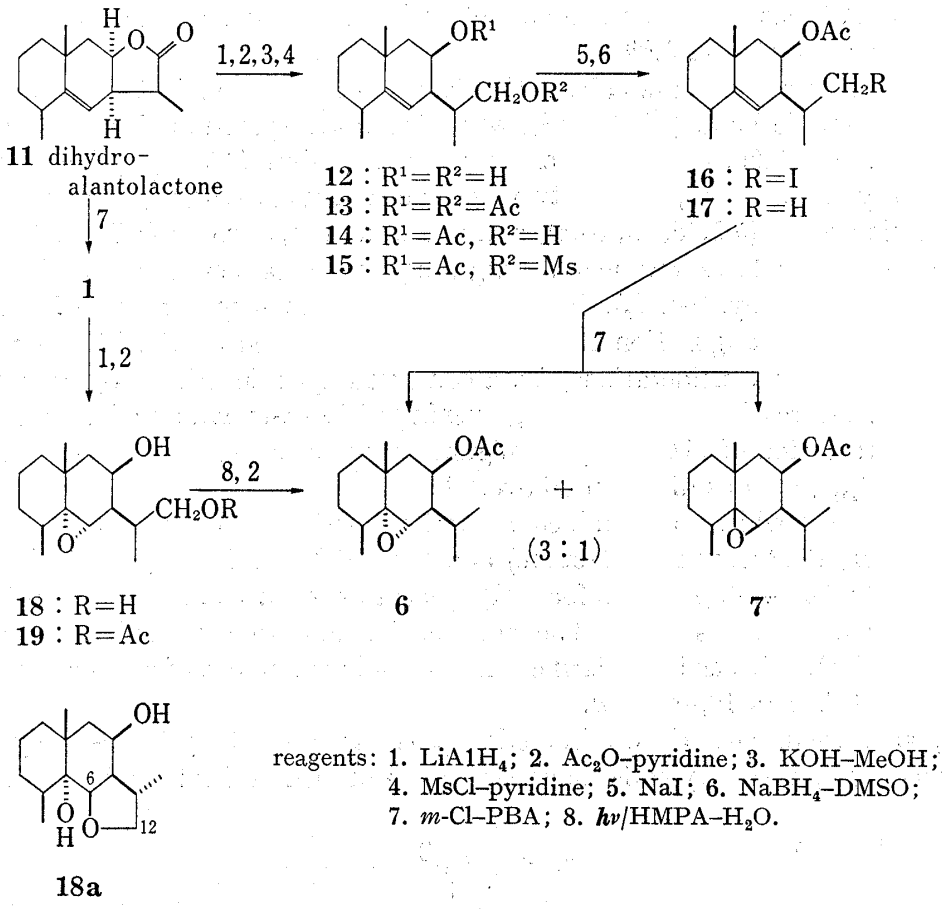


Chart 3

Acid Treatment of Four Epoxides (4, 5, 6, and 7)

Treatment of 5α,6α-epoxy-11βH-eudesman-8β,12-olide (**4**) with a formic acid–acetone (2:1) mixture[3b] furnished a transformation product (**20**, designated as A-2) in a 62% yield. The IR spectrum of A-2 shows absorption bands due to γ-lactone (1768 cm^{-1}) and ester (1715 cm^{-1}), whereas the PMR spectrum shows the presence of one tertiary methyl (δ 1.11, s, 5-CH_3),

8) In the PMR spectrum of **18a**, signals due to three protons attached to the ether ring are observed: a doublet ($J=4$ Hz) at δ 3.43 for 6-H, a doublet of doublet ($J=8$ and 4 Hz) at δ 3.24 for 12α-H, and a triplet ($J=8$ Hz) at δ 4.20 for 12β-H, and the geminal coupling constant of $|J_{12\alpha\text{-H},12\beta\text{-H}}|=8$ Hz suggests the ether ring to be a tetrahydrofuran ring.[9]

9) R.C. Cookson, T.A. Crabb, J.J. Frankel, and J. Hudec, *Tetrahedron, Suppl.* 7, 355 (1966).

10) H. Deshayes, J.P. Pete, C. Portella, and D. Scholler, *J. Chem. Soc. Chem. Commun.*, **1975**, 439.

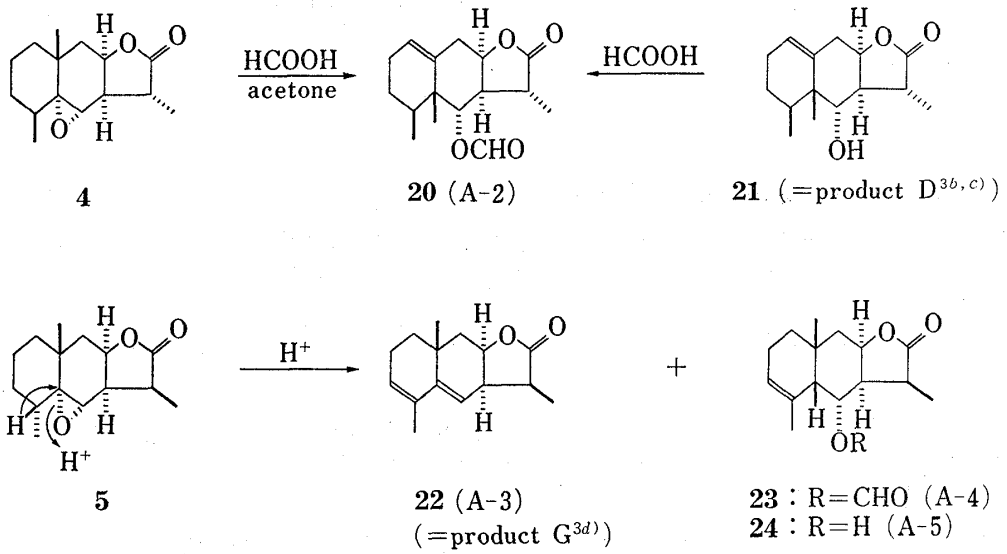
two secondary methyls (δ 0.86 and 1.34, both d, J=7 Hz, 4-CH_3 and 11-CH_3), one olefinic proton (δ 5.62, m, 1-H), and two methine protons of which one is geminal to the lactone ring (δ 4.49, d.t, J=11 and 7 Hz, 8-H) and another to the formyloxyl function (δ 5.27, d, J=3 Hz, 6-H), thus the structure **20** being presumed for A-2. The presumption has been verified by preparation of A-2 through formylation of **21** (=product D[3b,c]). It has been thus demonstrated that the configuration of 11-methyl (either β as in **1** or α as in **4**) could not be an essential factor for promoting the angular methyl migration of **1** or **4** under acid conditions.

Next, treatment of **5** under four different acid conditions (formic acid–acetone, boron trifluoride etherate–benzene, trifluoroacetic acid–chloroform, and *p*-toluenesulfonic acid monohydrate–chloroform)[5] was carried out monitoring reaction products by thin-layer and gas–liquid chromatography (TLC, GLC). As summarized in Table II, three products (designated respectively as A-3 (**22**), A-4 (**23**), and A-5 (**24**)) were obtained. Among these, the common product A-3 has been found to be identical to a dienic compound which was previously obtained as product G (**22**).[3d]

The IR spectrum of A-4 shows absorption bands ascribable to γ-lactone (1762 cm^{-1}), ester (1715 cm^{-1}), and double bond (1650 cm^{-1}), while the PMR spectrum shows the presence of one tertiary methyl (δ 1.06, s, 10-CH_3), one secondary methyl (δ 1.37, d, J=7 Hz, 11-CH_3), one olefinic methyl (δ 1.70, br.s, 4-CH_3), two methine protons (δ 4.78, m, 8-H and δ 5.53, br.s, 6-H), one olefinic proton (δ 5.58, m, 3-H), and one formyloxyl proton (δ 7.94, s). The spin-decoupling experiments have revealed a long-range coupling between the olefinic proton (3-H) and the olefinic methyl (4-CH_3), thus the 5β H-eudesmane-type structure **23** being assumed for A-4. The 5β-H configuration in **23** has been mainly based on the PMR signal pattern of 6β-H and mechanistic considerations, *i.e.* a concerted hydride shift of 4β-H in **5** to a carbonium cation at C-5 resulted from the ring-opening of 5α,6α-epoxide under acid conditions. In addition, the retention of 11β-methyl configuration in **23** has substantiated by its positive CD maximum ($[\theta]_{218}$+490) as discussed above.[5,6]

In the case of A-5 which was obtained under three acid conditions (Table II), the IR (3550 cm^{-1} for hydroxyl; 1762 cm^{-1} for γ-lactone) and the PMR (δ 1.73, d, J=1.5 Hz for 4-CH_3; δ 5.78, m, for 3-H; δ 4.24, d, J=2 Hz for 6-H) spectra have led us to presume A-5 (**24**) to be a desformyl derivative of A-4 (**23**). The presumption has been verified by formylation of A-5 to afford A-4 (**23**). It has been clarified that, on acid treatment of **5**, 4β-H (axial) is more readily shifted to C-5 than 10β-methyl.

Finally, acid treatment of two isomeric epoxides: 8β-acetoxy-5α,6α-epoxy-eudesmane (**6**) and 8β-acetoxy-5β,6β-epoxy-eudesmane (**7**) was examined as for **5**, and the compositions



4 **20** (A-2) **21** (=product D[3b,c])

5 **22** (A-3) (=product G[3d]) **23** : R=CHO (A-4) **24** : R=H (A-5)

Chart 4

Table II. Compositions of Reaction Products obtained by Treatment of **5** under Various Acid Conditions[a]

Acid conditions	Products		
	A-3(**22**)	A-4(**23**)	A-5(**24**)
HCOOH–acetone	22(16)[b]	44(36)[b]	—
BF_3-etherate–benzene	12 (9)[b]	—	62(51)[b]
CF_3COOH–$CHCl_3$	16	—	53
p-TsOH·H_2O–$CHCl_3$	41	—	39

a) The compositions (%) are based on GLC analyses.
b) The percentages given in the parentheses are the yields of isolated products.

of reaction products under four acid conditions are summarized in Table III. The spectral properties of the common product A-6 has led us to assume a 6-keto structure (**25**) for A-6. Thus, the IR spectrum shows the presence of an acetoxyl (1736 cm^{-1}) and a six-membered ring ketone (1713 cm^{-1}), whereas the PMR spectrum exhibits signals assignable to one tertiary methyl (δ 0.98, s, 10-CH_3), three secondary methyl (δ 0.78 and 0.79, each d, J=6 Hz, two 11-CH_3; δ 0.91, d, J=6 Hz, 4-CH_3), and a methine proton geminal to an acetoxyl (δ 5.46, m, 8-H), but lacks signals due to an olefinic proton and 6-H. In regard to the 5β-H configuration in A-6 (**25**), the mechanistic considerations (a hydride shift of 6β-H in **6**, pathway **a** in Chart 5) is suggestive. Furthermore, comparison of stereostructures (using Dreiding model) for **25** and its 5α-H isomer (**25a**) has led us to assume that **25a** may be less favored than **25** (more spatial interaction of axial residues in the former). The assumption has been supported by a negative CD maximum ($[\theta]_{298}$ −3300) of A-6 (**25**), which agrees with the octant projection of **25** either in a steroidal or nonsteroidal conformation. It should be mentioned here that the 6-keto compound (*e.g.* **25** from **6**) has not been obtained on acid treatment of 5α,6α-epoxides of eudesmane-type compounds (**1**, **4**, **5**) having a *cis*-γ-lactone moiety.

The structure of a minor dienic product A-7, which was obtained under two acid conditions, has been assigned as **26** having a heteroannular diene chromophore as shown by its ultraviolet (UV) spectrum (λ_{max} 235, 242, 250 nm). The PMR spectrum of A-7 is consistent with the eudesmane-type structure (**26**) as based on signals attributable to one tertiary methyl (δ 1.09, s, 10-CH_3), two secondary methyls (δ 0.90 and 1.02, each d, J=6 Hz, two 11-CH_3), one olefinic methyl (δ 1.81, d, J=1.5 Hz, 4-CH_3), one methine proton geminal to an acetoxyl (δ 5.27, m, 8-H), and two olefinic protons (δ 5.40—5.60, m, 3-H and 6-H). The reaction pathway from **6** to **26** (pathway **b**, Chart 5) seems to be similar as in the formation of product G (**22**) from **1**.[3]

The IR spectrum of another minor product A-8 (**27**), which was obtained under two acid conditions, shows the presence of hydroxyl (3630 cm^{-1}), acetoxyl (1722 cm^{-1}), and a terminal methylene function (1640, 900 cm^{-1}). In the PMR spectrum of **27**, are observed signals ascribable to three secondary methyls (δ 0.93 and 1.10, each d, J=7 Hz, two 11-CH_3; δ 1.01, d, J=6 Hz, 4-CH_3), two methine protons of which one is geminal to an acetoxyl (δ 5.12, m, 8-H) and another is a carbinyl proton (δ 3.94, d, J=11 Hz, 6-H), terminal methylene protons δ 4.80, br.s, 15-H_2), and ring methylene protons (δ 2.36, m, 9-H_2). In the spin-decoupling experiments (Table IV), signals due to ring methylene protons (δ 2.36, 9-H_2) have been disclosed to be in long-range couplings between those of terminal methylene protons. Based on these findings, a spiro[4.5]decane structure (**27**) has been proposed for A-8. The formation process is presumed to proceed through pathway **c** (Chart 5) in which the 1-10 bond in **6** shifts from β-side to C-5, since, for an α-side shift, a severe interaction between 4β-CH_3 and 10β-CH_3 would be resulted in the intermediate.

The structure of A-9 has been assigned as **28**. As shown in Table III, A-9 was obtained under three acid conditions in moderate yields. The IR spectrum of A-9 (**28**) lacks the ace-

toxyl absorption band, but the UV spectrum discloses the presence of a benzenoid chromophore in A-9 by a characteristic triplet maxima at 261, 267, and 274 nm. The PMR spectrum of A-9 exhibits signals due to four methyls, among which three are aliphatic secondary (δ 1.14, d, J=7 Hz, 1-CH_3; δ 1.19 and 1.28, each d, J=7 Hz, 5-$CH(C\underline{H}_3)_2$ and one attaches to an aromatic ring (δ 2.16, s, 8-CH_3), and signals of two aromatic protons (2H at δ 6.97, s, 6-H, 7-H). Based on these spectral properties and mechanistic considerations for probable formation of A-9 (**28**) *via* A-8 (**27**), a tetraline-type structure (**28**) has been proposed for A-9 and presumed to be more favored than **28a**. The appearance of two aromatic proton signals as a two-proton singlet in the PMR spectrum of A-9 (**28**) has a precedent analogy in the PMR spectrum of a cadinane-type derivative (**29**).[11] It has become apparent that acid treatment of **6** furnishes no eremophilane-type compound.

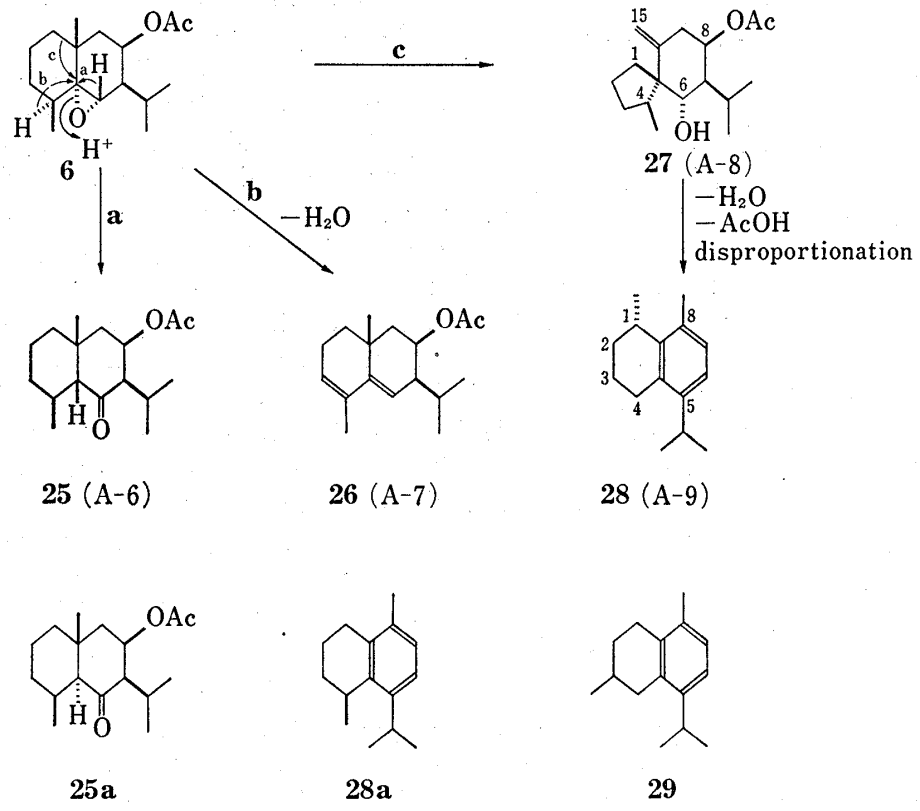


Chart 5

Table III. Compositions of Reaction Products obtained by Treatment of **6** under Various Acid Conditions[a]

Acid conditions	Products			
	A-6(**25**)	A-7(**26**)	A-8(**27**)	A-9(**28**)
HCOOH–acetone	30	7	6	16
BF_3-etherate–$CHCl_3$	60	—	—	—
CF_3COOH–$CHCl_3$	45(34)[b]	5(3)[b]	4(3)[b]	25(20)[b]
p-TsOH·H_2O–$CHCl_3$	26	—	—	44

a) The compositions (%) are based on GLC analyses.
b) The percentages given in the parentheses are the yields of isolated products.

11) B.N. Joshi, R. Seshadri, K.K. Chakravarti, and S.C. Bhattacharyya, *Tetrahedron*, **20**, 2911 (1964).

Table IV. Spin-Decoupling Experiments of A-8 (**26**)

Decoupled protons (δ)	Irradiated at δ		
	5.12(8-H)	2.36(9-H_2)	4.82(15-H_2)
8-H(5.12, m)	—	Doublet(J=2 Hz)	
9-H_2(2.36, m)	Varied	—	Varied
15-H_2(4.82, br.s)		Singlet	—

Treatment of **7** under four acid conditions as for **5** and **6** gave three products: A-7 (**26**), A-10 (**30**), and A-11 (**31**) as summarized in Table V, among which A-7 was identified by direct comparison with the one (**26**) obtained from **6.**

A-10 (**30**) and A-11 (**31**) are isomeric each other. The IR spectrum of A-10 shows the presence of hydroxyl (3600 cm^{-1}), acetoxyl (1739 cm^{-1}), and a terminal methylene function (1645, 897 cm^{-1}) while that of A-11 exhibits absorption bands due to hydroxyl (3600 cm^{-1}), acetoxyl (1735 cm^{-1}), and double bond (1643 cm^{-1}). The PMR spectra of both also disclose their structural resemblance. Besides signals due to one tertiary methyl (10-CH_3), two secondary methyls (at C-11), and two methine protons respectively geminal to an acetoxyl (8-H) and a hydroxyl (6-H), signals ascribable to terminal methylene protons (δ 4.91 and 5.14, 1H each, br.s, 14-H_2) are observed in A-10 (**30**) while signals due to a long-range coupled olefinic methyl

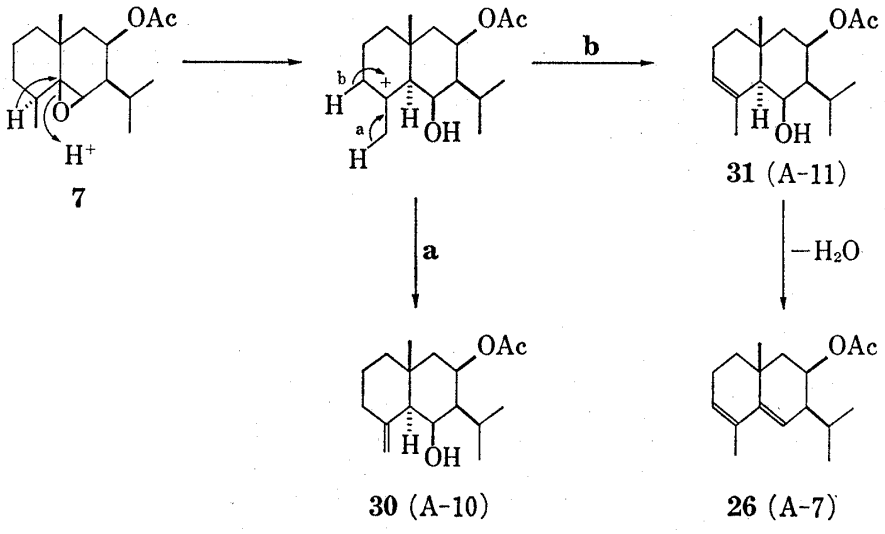


Chart 6

Table V. Compositions of Reaction Products obtained by Treatment of **7** under Various Acid Conditions[a)]

Acid conditions	Products	
	A-7(**26**)	A-10(**30**) + A-11(**31**)[b)]
HCOOH–acetone	42	45
BF_3-etherate–benzene	25(22)[c)]	60(**30**=10, **31**=45)[c)]
CF_3COOH–$CHCl_3$	9	79
p-TsOH·H_2O–ether	61	12

a) The compositions (%) are based on GLC analyses.
b) The yields of A-10 and A-11 are given in the combined values.
c) The percentages given in the parentheses are the yields of isolated products.

(δ 1.84, d, J=1 Hz, 4-CH_3) and an olefinic proton (δ 5.39, m, 3-H) are observed in A-11 (**31**). Based on these spectral properties of both and the mechanistic viewpoint (pathway **a** and **b** in Chart 6), A-10 and A-11 have been respecively assigned the eudesmane-type structures **30** and **31**, in which the 5α-H configuration follows a presumable hydride shift of 4α-H in **7** towards a carbonium cation at C-5 resulted from the epoxide ring opening. Here again, no eremophilane-type compound was obtained.

Based on the accumulated evidence mentioned above in combination with our previous results obtained from **3**,[5] the essential factors for the successful angular methyl migration experienced in **1** have been demonstrated as below. 1) Since acid treatment of **4** has readily afforded an eremophilane-type compound A-2 (**20**), the spatial interaction conceivable between 10-methyl and 11β-methyl in **1** would not be indispensable. 2) Since no eremophilane-type compound has been produced on acid treatment of **3**,[5] **5**, **6**, and **7**, the combinations of the following factors seem to be important: a) the presence of 5α,6α-epoxide which arises a carbonium cation at C-5 by the ring opening, b) the spatial interaction between 10-methyl and 4β-methyl which would bring about distortion of the ring A, thus making **1** thermodynamically unstable and finally c) the presence of *cis*-γ-lactone which possibly settles the boat-like conformation of the ring B, thus favoring the 1,2-shift of 10-methyl to the carbonium cation induced at C-5 (*cf.* **i**).

The fact, that a 5α,6α-epoxy-eudesmane having a *cis*-γ-lactone moiety attached to C-7 and C-8 has been transformed to eremophilanolides, while the one lacking the lactone moiety would not give any eremophilane-type compound, has led us to presume that the γ-lactone ring would function for settling the conformation of the ring B during the angular methyl migration. This presumed function is reminiscent of an enzymatic mold, which would be probably playing an important role in the reaction pathway *in vivo* during the biogenetic angular methyl migration from a precursory eudesmane-type sesquiterpene leading to an eremophilane-type counterpart.

Experimental[12]

Potassium Carbonate Treatment of 1——To a stirred mixture of **1** (200 mg) in dry toluene (12 ml) was added dry K_2CO_3 (2 g), and the stirred total mixture was heated under reflux for 10 hr. After cooling, the reaction mixture was filtered to remove K_2CO_3, and the filtrate was evaporated under reduced pressure. A white powder (192 mg) thus obtained was subjected to preparative TLC (*n*-hexane–$CHCl_3$–MeOH=40: 50: 1, developing twice) to give **1** (136 mg, recovered) and **4** (28 mg). **4**, mp 155°, colorless needles (recrystallized from *n*-hexane–acetone), $[\alpha]_D^{20}$ −31° (c=0.50, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.68; H, 8.82. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1766, 987. CD (c=0.050, MeOH): $[\theta]_{216}^{22}$ −1580 (neg. max.), $[\theta]_{250}^{22}$ 0. PMR ($CDCl_3$) δ: 1.12 (3H, d, J=7 Hz, 4-CH_3), 1.18 (3H, s, 10-CH_3), 1.42 (3H, d, J=7 Hz, 11-CH_3), 2.86 (1H, br.s, $W_{h/2}$=3 Hz, 6-H), 4.66 (1H, m, 8-H). MS *m/e* (%): 250 (M^+, 9), 126 (100).

***p*-Toluenesulfonic Acid Treatment of 8**——To a solution of **8** (1.02 g) in glacial acetic acid (10 ml) was added *p*-TsOH·H_2O (150 mg), and the total solution was heated under reflux for 1.5 hr. After cooling, the reaction mixture was treated with ice-water and extracted with EtOAc. The EtOAc extract was then successively washed with 5% aq. $NaHCO_3$ and water, and dried over $MgSO_4$. Evaporation of the solvent gave a colorless oily product (1.0 g) which was purified by column chromatography (silica gel 70 g, *n*-hexane–ether=20: 1) and preparative TLC (*n*-hexane–ether=3: 2, developing twice) to furnish **9** (650 mg)[5] and **10** (140 mg). **10**, mp 150°, colorless needles (recryst. from EtOH), $[\alpha]_D^{20}$ +23° (c=1.0, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{22}O_2$: C, 76.88; H, 9.46. Found: C, 76.55; H, 9.41. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1760, 1665. PMR ($CDCl_3$) δ: 1.00 (3H, d, J=7 Hz, 4-CH_3), 1.18 (3H, s, 10-CH_3), 1.22 (3H, d, J=7 Hz, 11-CH_3), 2.84 (1H, quintet, J=7 Hz, 11-H), 2.93 (1H, m, 7-H), 4.67 (1H, m, 8-H), 5.07 (1H, t, J=3 Hz, 6-H). MS *m/e* (%): 234 (M^+, 26), 145 (100).

Epoxidation of 10 giving 5——To a solution of **10** (135 mg) in $CHCl_3$ (2 ml) was added a solution of *m*-chloroperbenzoic acid (135 mg) in $CHCl_3$ (10 ml), and the total solution was kept stirring at room temperature for 40 min, treated with 10% aq. Na_2SO_3, washed successively with 5% aq. $NaHCO_3$ and water, and worked up in the usual manner. **5** (115 mg), mp 116°, colorless needles (recryst. from *n*-hexane), $[\alpha]_D^{15}$ −55° (c=0.60,

12) The instruments used for obtaining the physical data and experimental conditions for various chromatography were same as in our previous paper.[1,3,5]

$CHCl_3$). *Anal.* Calcd. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.68; H, 8.82. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1765, 975. PMR ($CDCl_3$) δ: 0.77 (3H, d, J=7 Hz, 4-CH_3), 1.16 (3H, s, 10-CH_3), 1.31 (3H, d, J=7 Hz, 11-CH_3), 3.11 (1H, br.s, $W_{h/2}$=3 Hz, 6-H), 5.54 (1H, m, 8-H). MS *m/e* (%): 250 (M^+, 3), 126 (100).

$LiAlH_4$ Reduction of 11 giving 12——To a stirred suspension of $LiAlH_4$ (300 mg) in dry ether (50 ml) was added **11** (1.9 g) in small portions, and the total mixture was kept stirring at room temperature for 1.5 hr, treated successively with ether saturated with water and 10% aq. H_2SO_4, and extracted with ether. The ether extract was washed with sat. aq. $NaHCO_3$ and water, and worked up in the usual manner to give **12** (1.81 g). **12**, mp 88°, colorless prisms (recryst. from ether), $[\alpha]_D^{26}$ +8.1° (c=1.1, $CHCl_3$). *Anal.* Calcd. for $C_{15}H_{26}O_2$: C, 75.58; H, 11.00. Found: C, 75.71; H, 10.97. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3620, 3418, 1620. PMR ($CDCl_3$) δ: 1.04 (3H, d, J=8 Hz, 11-CH_3), 1.17 (3H, d, J=8 Hz, 4-CH_3), 1.32 (3H, s, 10-CH_3), 3.16 (2H, br.s, OH×2, D_2O exchangeable), 3.48, 3.69 (1H, each, AB part in ABX, $|J_{AB}|$=11 Hz, 12-H_2), 4.09 (1H, m, 8-H), 5.22 (1H, d, J=2 Hz, 6-H). MS *m/e* (%): 238 (M^+, 3), 105 (100).

Acetylation of 12 giving 13——A solution of **12** (3.0 g) in pyridine (35 ml) was treated with Ac_2O (20 ml) and the total solution was heated at 100° for 1.5 hr, poured into ice-water, and extracted with ether. The ether extract was then successively washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and water, and worked up in the usual manner to give **13** (4.0 g). **13**, colorless glassy, $[\alpha]_D^{15}$ +5.0° (c=1.0, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1737, 1648, 1240. PMR ($CDCl_3$) δ: 0.96 (3H, d, J=6 Hz, 11-CH_3), 1.14 (3H, d, J=7 Hz, 4-CH_3), 1.19 (3H, s, 10-CH_3), 2.02, 2.04 (3H each, both s, $OCOCH_3$×2), 4.03, 4.23 (1H. each, AB part in ABX, $|J_{AB}|$=11 Hz, 12-H_2), 5.17 (1H, m, 8-H), 5.29 (1H, d, J=2 Hz, 6-H). MS *m/e* (%): 322 (M^+, 1), 202 (100). High resolution MS *m/e*: Found 322.214; Calcd. for $C_{19}H_{30}O_4$ (M^+) 322.214.

Partial Hydrolysis of 13 giving 14——A solution of **13** (3.95 g) in 1% KOH–MeOH (87 g) was left standing at 0° for 2 hr and poured into ice-water. After removing MeOH under reduced pressure, the aqueous mixture was neutralized with 7% aq. HCl and extracted with ether. The ether extract was then successively washed with aq. NaCl and water, and worked up in the usual manner. The oily product (3.3 g) thus obtained was purified by column chromatography (silica gel 100 g, *n*-hexane–ether=3:1) to give **14** (2.70 g). **14**, colorless oil, $[\alpha]_D^{15}$ −9.3° (c=0.93, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3435, 1740, 1650, 1250. PMR ($CDCl_3$) δ: 0.97 (3H, d, J=6 Hz, 11-CH_3), 1.14 (3H, d, J=6 Hz, 4-CH_3), 1.20 (3H, s, 10-CH_3), 2.02 (3H, s, $OCOCH_3$), 3.65, 3.75 (1H each, AB part in ABX, $|J_{AB}|$=11 Hz, 12-H_2), 5.18 (1H, m, 8-H), 5.34 (1H, d, J=2 Hz, 6-H). MS *m/e* (%): 280 (M^+, 1), 189 (100). High resolution MS *m/e*: Found 280.203; Calcd. for $C_{17}H_{28}O_3$ (M^+) 280.204.

Mesylation of 14 giving 15——A solution of **14** (2.85 g) in pyridine (10 ml) was treated with mesyl chloride (1 ml), left standing at room temperature for 3 hr, poured into ice-water, and extracted with ether. The ether extract was successively washed with 5% aq. HCl, sat. aq. $NaHCO_3$, and water, and worked up in the usual manner to give **15** (3.25 g). **15**, colorless oil, $[\alpha]_D^{15}$ +12° (c=0.79, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1734, 1355, 1245, 1175. PMR ($CDCl_3$) δ: 1.06 (3H, d, J=7 Hz, 11-CH_3), 1.14 (3H, d, J=7 Hz, 4-CH_3), 1.19 (3H, s, 10-CH_3), 2.03 (3H, s, $OCOCH_3$), 3.00 (3H, s, OSO_2CH_3), 4.21, 4.38 (1H each, AB part in ABX, $|J_{AB}|$=10 Hz, 12-H_2), 5.19 (1H, m, 8-H), 5.27 (1H, d, J=2 Hz, 6-H). MS *m/e* (%): 358 (M^+, 1), 202 (100). High resolution MS *m/e*: Found 358.180; Calcd. for $C_{18}H_{26}O_5S$ (M^+) 358.181.

NaI Treatment of 15 giving 16——To a stirred solution of **15** (3.09 g) in acetone (10 ml) was added dropwise a solution of NaI (7.30 g) in acetone (25 ml), and the stirred total mixture was heated under reflux for 4 hr. After cooling, the reaction mixture was evaporated under reduced pressure, and the residue was extracted with ether. The ether extract was then successively washed with 5% aq. $Na_2S_2O_3$, aq. NaCl, and water, and worked up in the usual manner to give **16** (3.22 g). **16**, colorless oil, $[\alpha]_D^{15}$ +15° (c=1.6, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1732, 1650, 1240. PMR ($CDCl_3$) δ: 1.00 (3H, d, J=6 Hz, 11-CH_3), 1.16 (3H, d, J=6 Hz, 4-CH_3), 1.19 (3H, s, 10-CH_3), 2.03 (3H, s, $OCOCH_3$), 3.30, 3.46 (1H each, AB part in ABX, $|J_{AB}|$=10 Hz, 12-H_2), 5.16 (1H, m, 8-H), 5.22 (1H, d, J=2 Hz, 6-H). MS *m/e* (%): 390 (M^+, 9), 161 (100). High resolution MS *m/e*: Found 390.105; Calcd. for $C_{17}H_{27}O_2I$ (M^+) 390.105.

$NaBH_4$ Reduction of 16 giving 17——To a solution of **16** (3.05 g) in DMSO (20 ml) was added dropwise a solution of $NaBH_4$ (0.89 g) in DMSO (60 ml), and the total solution was kept stirring at 20° for one hour, and heated under reflux for 15 min. After cooling, the reaction mixture was poured into ice-water, neutralized with 5% aq. HCl, and extracted with ether. The ether extract was then washed successively with aq. NaCl solution and water, and worked up in the usual manner to give **17** (2.05 g). **17**, colorless oil, $[\alpha]_D^{16}$ −15° (c=1.2, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1740, 1650, 1245. PMR ($CDCl_3$) δ: 0.88, 0.98 (3H each, d, J=7 Hz, 11-CH_3×2), 1.16 (3H, d, J=8 Hz, 4-CH_3), 1.18 (3H, s, 10-CH_3), 2.00 (3H, s, $OCOCH_3$), 5.18 (1H, m, 8-H), 5.33 (1H, br.s, 6-H). MS *m/e* (%): 264 (M^+, 7), 105 (100). High resolution MS *m/e*: Found 264.208; Calcd. for $C_{17}H_{28}O_2$ (M^+) 264.209.

Epoxidation of 17 giving 6 and 7——To a solution of **17** (102 mg) in CH_2Cl_2 (3 ml) was added dropwise a solution of *m*-chloroperbenzoic acid (100 mg) in CH_2Cl_2 (5 ml) and the total solution was kept stirring at 0° for 40 min, treated with 10% aq. Na_2SO_3, and extracted with ether. The ether extract was then washed with water and worked up in the usual manner. The oily product (93 mg) thus obtained was subjected to preparative TLC (*n*-hexane–$CHCl_3$=1:2) to give **6** (65 mg) and **7** (20 mg). **6**, colorless glassy, $[\alpha]_D^{16}$ −33° (c=0.75, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1739, 1244. PMR ($CDCl_3$) δ: 0.97, 1.07, 1.14 (3H each, d, J=6 Hz, 4-CH_3, 11-CH_3×2), 1.24 (3H, s, 10-CH_3), 2.00 (3H, s, $OCOCH_3$), 2.84 (1H, br.s, 6-H), 5.00 (1H, m, 8-H). MS *m/e* (%): 280 (M^+, 4), 109 (100). High resolution MS *m/e*: Found 280.203; Calcd. for $C_{17}H_{28}O_3$ (M^+) 280.203.

7, colorless glassy, $[\alpha]_D^{22}$ +63° (c=0.68, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1730, 1255. PMR ($CDCl_3$) δ: 1.03, 1.09, 1.10 (3H each, d, J=6 Hz, 4-CH_3, 11-CH_3×2), 1.11 (3H, s, 10-CH_3), 2.00 (3H, s, $OCOCH_3$), 2.93 (1H, d, J=4 Hz, 6-H), 5.05 (1H, d.d.d, J=12, 6 and 3 Hz, 8-H). MS m/e (%): 280 (M^+, 6), 43 (100). High resolution MS m/e: Found 280.203; Calcd. for $C_{17}H_{28}O_3$ (M^+) 280.203.

$LiAlH_4$ Reduction of 1 (giving 18) followed by Acetylation giving 19——To a cooled suspension of $LiAlH_4$ (130 mg) in dry ether (40 ml) was added **1** (1.0 g) and the total mixture was kept stirring at −20° for 40 min, treated with ether saturated with water, and extracted with ether. After usual work-up, **18** (870 mg) thus obtained was acetylated with pyridine (9 ml) and Ac_2O (1 ml) at 0° overnight. The reaction mixture was poured into ice-water, and extracted with ether. The ether extract was then washed successively with 5% aq. HCl, 5% aq. $NaHCO_3$, and water, and worked up in the usual manner. The product (950 mg) was then purified by column chromatography (silica gel 20 g, $CHCl_3$–ether=5: 1) to give **19** (464 mg). **19**, mp 111.5—112.5°, colorless needles (recryst. from acetone), $[\alpha]_D^{26}$ −20° (c=0.56 $CHCl_3$). *Anal.* Calcd. for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.85; H, 9.49. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3615, 1733. PMR ($CDCl_3$) δ: 1.16, 1.17 (3H each, d, J=7 Hz, 4-CH_3, 11-CH_3), 1.39 (3H, s, 10-CH_3), 2.07 (3H, s, $OCOCH_3$), 2.89 (1H, d, J=0.5 Hz, 6-H), 4.05 (1H, m, 8-H), 4.15, 4.45 (1H each, AB part in ABX, $|J_{AB}|$=10 Hz, 12-H_2). MS m/e (%): 296 (M^+, 1), 126 (100).

Photoreduction of 19 followed by Acetylation giving 6——A solution of **19** (50 mg) in an HMPA–water (95: 5) mixture (10 ml) was put in a quartz tube and irradiated with a 30 W low pressure mercury lamp (Eikosha PIL-30) for 60 hr. The reaction mixture was poured into ice-water and extracted with ether. After washing with water, the ether extract was worked up in the usual manner to give an oily product (35 mg), which was acetylated with Ac_2O (0.3 ml) and pyridine (0.4 ml) at 40° for 2 days. The reaction mixture was poured into ice-water, extracted with ether, and the ether extract was then washed successively with 5% aq. HCl, 5% aq. $NaHCO_3$, and water, and worked up in the usual manner. The oily product (35 mg) thus obtained was purified by preparative TLC ($CHCl_3$–ether=5: 1) to give a product (15 mg) which was identified with **6** by TLC (n-hexane–acetone=40: 1, n-hexane–$CHCl_3$=1: 2, $CHCl_3$–ether=5: 1), IR (film), GLC, and PMR ($CDCl_3$).

Treatment of 4 with HCOOH–Acetone (2: 1) giving 20 (A-2)——A solution of **4** (50 mg) in a mixture of freshly distilled acetone (6 ml) and 99% HCOOH (12 ml) was heated under reflux under argon atmosphere for 1.5 hr. After cooling, the reaction mixture was treated with water (10 ml), neutralized with 5% aq. KOH, and extracted with ether. The ether extract was then washed with water and worked up in the usual manner to give an oily product (46 mg). Purification of the product by preparative TLC ($CHCl_3$–ether=5: 1) gave A-2 (**20**) (34 mg, 62%), colorless glassy, $[\alpha]_D^{20}$ −31° (c=0.50, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1768, 1715. PMR ($CDCl_3$) δ: 0.86 (3H, d, J=7 Hz, 4-CH_3), 1.11 (3H, s, 5-CH_3), 1.34 (3H, d, J=7 Hz, 11-CH_3), 4.49 (1H, d.t, J=11 and 7 Hz, 8-H), 5.27 (1H, d, J=3 Hz, 6-H), 5.62 (1H, m, 1-H). MS m/e (%): 278 (M^+, 1), 83 (100). High resolution MS m/e: Found 278.151; Calcd. for $C_{16}H_{22}O_4$ (M^+) 278.152.

Formylation of 21 (Product D) giving 20——A solution of **21** (20 mg) in freshly distilled acetone (1 ml) and 99% HCOOH (2 ml) was heated under reflux for one hour. After cooling, the reaction mixture was neutralized with 5% aq. $NaHCO_3$ and extracted with ether. After washing with water, working up of the ether solution in the usual manner gave a single product (16 mg), which was identified with A-2 (**20**) by TLC ($CHCl_3$–ether=5: 1), GLC, and PMR.

Treatment of 5 with HCOOH–Acetone (2: 1) giving 22 and 23——A solution of **5** (100 mg) in freshly distilled acetone (1.3 ml) and 99% HCOOH (2.6 ml) was heated under reflux under argon atmosphere for one hour. After cooling, the reaction mixture was diluted with water, neutralized with 5% aq. $NaHCO_3$, and extracted with ether. After washing with water, working up of the ether extract gave an oily product (104 mg). Column chromatography of the product (silica gel 10 g, n-hexane–acetone=12: 1) gave A-3 (**22**) (15 mg, 16%) and A-4 (**23**) (40 mg, 36%). A-3 (**22**) thus obtained was identified with product $G^{3d)}$ by TLC ($CHCl_3$–ether=5: 1), GLC, and PMR. A-4 (**23**), mp 79—80°, colorless needles (recryst. from n-hexane–acetone), $[\alpha]_D^{20}$ −104° (c=0.50, $CHCl_3$). *Anal.* Calcd. for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.01; H, 7.90. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1762, 1715, 1650. CD (c=0.128, MeOH): $[\theta]_{218}^{23}$ +490 (pos. max.), $[\theta]_{245}^{23}$ 0. PMR ($CDCl_3$) δ: 1.06 (3H, s, 10-CH_3), 1.37 (3H, d, J=7 Hz, 11-CH_3), 1.70 (3H, br.s, 4-CH_3), 2.67 (1H, m, 7-H), 3.03 (1H, m, 11-H), 4.78 (1H, m, 8-H), 5.53 (1H, br.s, 6-H), 5.58 (1H, m, 3-H), 7.94 (1H, s, OCHO). MS m/e (%): 278 (M^+, 1), 143 (100).

Treatment of 5 with BF_3-etherate in Benzene giving 22 and 24——To a solution of **5** (100 mg) in benzene (20 ml) was added BF_3-etherate (0.25 ml), and the total solution was kept stirring at room temperature under argon atmosphere for 10 min and treated with 5% aq. $NaHCO_3$. The benzene layer was then washed with water, and worked up in the usual manner to give an oily product (91 mg). Column chromatography (silica gel 10 g, n-hexane–acetone=10: 1) of the product gave A-3 (**22**) (8.3 mg, 10%) (=product $G^{3d)}$) and A-5 (**24**) (51 mg, 51%). **24**, colorless glassy, $[\alpha]_D^{20}$ −9° (c=0.3, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3550, 1762. CD (c=0.150, MeOH): $[\theta]_{222}^{23}$ +1060 (pos. max.), $[\theta]_{240}^{23}$ 0. PMR ($CDCl_3$) δ: 1.00 (3H, s, 10-CH_3), 1.28 (3H, d, J=7 Hz, 11-CH_3), 1.73 (3H, d, J=1.5 Hz, 4-CH_3), 4.24 (1H, d, J=2 Hz, 6-H), 4.83 (1H, d.t, J=6 and 4 Hz, 8-H), 5.78 (1H, m, 3-H). MS m/e (%): 250 (M^+, 14), 143 (100). High resolution MS m/e: Found 250.157; Calcd. for $C_{15}H_{22}O_3$ (M^+) 250.157.

Treatment of 5 with CF_3COOH-$CHCl_3$——A solution of **5** (15 mg) in $CHCl_3$ (1 ml) was treated with CF_3COOH (0.5 ml), and heated under reflux under argon atmosphere for one hour. After cooling, the reaction mixture was neutralized with 5% aq. $NaHCO_3$, and the $CHCl_3$ layer was treated in the usual manner to give a product (13 mg). GLC of the product (SE-30, 1 m×3 mm, column temp. 200°) disclosed the composition of **22** and **24** as shown in Table II.

Treatment of 5 with *p*-TsOH·H_2O-$CHCl_3$——A solution of **5** (15 mg) in $CHCl_3$ (1 ml) was treated with *p*-TsOH·H_2O (10 mg) and heated under reflux under argon atmosphere for one hour. After cooling, the reaction mixture was neutralized with 5% aq. $NaHCO_3$ and the $CHCl_3$ layer was worked up in the usual manner. The product (12 mg) was subjected to GLC analyses as above to disclose the composition of **22** and **24** as shown in Table II.

Formylation of 24 giving 23——A solution of **24** (10 mg) in freshly distilled acetone (0.3 ml) and 99% HCOOH (0.6 ml) was heated under reflux for 1.5 hr. After cooling, the reaction mixture was neutralized with 5% aq. $NaHCO_3$ and extracted with ether. After washing with water, working up of the ether extract gave a single product (8 mg), which was identified with A-4 (**23**) by TLC ($CHCl_3$–ether=5:2) and GLC.

Treatment of 6 with CF_3COOH-$CHCl_3$ giving 25, 26, 27, and 28——A solution of **6** (200 mg) in CF_3COOH–$CHCl_3$ (1:50) (100 ml) was heated under reflux under argon atmosphere for 5 min. After cooling, the reaction mixture was neutralized with 5% aq. $NaHCO_3$ and the $CHCl_3$ layer was worked up in the usual manner to give an oily product (197 mg). Column chromatography (silica gel 10 g, *n*-hexane–acetone=10:1) of the product gave A-6 (**25**) (68 mg, 34%), A-7 (**26**) (6 mg, 3%), A-8 (**27**) (6 mg, 3%), and A-9 (**28**) (30 mg, 20%). A-6 (**25**), mp 119—120°, colorless plates (recryst. from *n*-hexane), $[\alpha]_D^{22}$ −40° (*c*=0.17, $CHCl_3$). *Anal.* Calcd. for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 73.11; H, 10.34. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1736, 1713. CD (*c*=0.150, MeOH): $[\theta]_{298}^{31}$ −3300 (neg. max.), $[\theta]_{330}^{31}$ 0. PMR ($CDCl_3$) δ: 0.78, 0.79 (3H each, d, *J*=6 Hz, 11-CH_3×2), 0.91 (3H, d, *J*=6 Hz, 4-CH_3), 0.97 (3H, s, 10-CH_3), 1.98 (3H, s, $OCOCH_3$), 5.46 (1H, m, 8-H). MS *m/e* (%): 280 (M^+, 4), 109 (100). A-7 (**26**), colorless glassy, $[\alpha]_D^{22}$ −27° (*c*=0.72, $CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1731. UV $\lambda_{max}^{dioxane}$ nm (ε): 235 (9600), 242 (10000), 250 (9100). PMR ($CDCl_3$) δ: 0.90, 1.02 (3H each, d, *J*=6 Hz, 11-CH_3×2), 1.09 (3H, s, 10-CH_3), 1.82 (3H, d, *J*=1.5 Hz, 4-CH_3), 2.03 (3H, s, $OCOCH_3$), 5.27 (1H, m, 8-H), 5.40—5.60 (2H, m, 3-H, 6-H). MS *m/e* (%): 262 (M^+, 22), 202 (100). High resolution MS *m/e*: Found 262.193; Calcd. for $C_{17}H_{26}O_2$ (M^+) 262.193. A-8 (**27**), mp 120—122°, colorless needles (*n*-hexane–EtOH), $[\alpha]_D^{22}$ −94° (*c*=0.16, $CHCl_3$). *Anal.* Calcd. for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.64; H, 10.28. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 1732, 1642, 900. PMR ($CDCl_3$) δ: 0.93 (3H, d, *J*=7 Hz, 11-CH_3), 1.01 (3H, d, *J*=6 Hz, 4-CH_3), 1.10 (3H, d, *J*=7 Hz, 11-CH_3), 1.99 (3H, s, $OCOCH_3$), 2.36 (2H, m, 9-H_2), 3.94 (1H, d, *J*=1 Hz, 6-H), 4.82 (2H, br.s, 15-H_2), 5.12 (1H, m, 8-H). MS *m/e* (%): 280 (M^+, 1), 43 (100). A-9 (**28**), colorless glassy, $[\alpha]_D^{22}$ −36° (*c*=0.13, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 1600, 825. UV λ_{max}^{hexane} nm (ε): 261 (270), 267 (290), 274 (230). PMR ($CDCl_3$) δ: 1.14 (3H, d, *J*=7 Hz, 1-CH_3), 1.19, 1.28 (3H each, d, *J*=7 Hz, 5-CH($C\underline{H}_3$)$_2$), 1.70—1.90 (4H, m, 2-H_2, 3-H_2), 2.16 (3H, s, 8-CH_3), 2.40—2.80 (2H, m, 4-H_2), 3.00—3.40 (2H, m, 1-H, 5-C$\underline{H}$(CH_3)$_2$), 6.97 (2H, s, 6-H, 7-H). MS *m/e* (%): 202 (M^+, 45), 187 (100). High resolution MS *m/e*: Found 202.170; Calcd. for $C_{15}H_{22}$ (M^+) 202.172.

Treatment of 6 with HCOOH-Acetone (1:2)——A solution of **6** (10 mg) in freshly distilled acetone (2 ml) and 99% HCOOH (1 ml) was heated under reflux under argon atmosphere for 20 min. After cooling, the reaction mixture was poured into ice-water and extracted with ether. The ether extract was then washed with 5% aq. $NaHCO_3$ and water, and worked up in the usual manner. The product (10 mg) was subjected to GLC analysis (SE-30, 1 m×3 mm, column temp. 200°) to disclose the composition of **25**, **26**, **27**, and **28** as shown in Table III.

Treatment of 6 with BF_3-etherate-$CHCl_3$——A solution of **6** (10 mg) in $CHCl_3$ (5 ml) was treated with BF_3-etherate (0.05 ml) and heated under reflux under argon atmosphere for 5 min. After cooling, the reaction mixture was neutralized with 5% aq. $NaHCO_3$ and the $CHCl_3$ layer was washed with water and worked up in the usual manner to give a product (9 mg). GLC analysis (as above) of the product disclosed the composition of the product (**25**) as given in Table III.

Treatment of 6 with *p*-TsOH·H_2O-$CHCl_3$——A solution of **6** (10 mg) in $CHCl_3$ (1.5 ml) was treated with *p*-TsOH·H_2O (6 mg) and heated under reflux under argon atmosphere for 15 min. After cooling, the reaction mixture was worked up as above to give a product (9 mg). GLC of the product showed the composition of the product (**25**, **28**) as given in Table III.

Treatment of 7 with BF_3-etherate-Benzene giving 26, 30, and 31——To a solution of **7** (128 mg) in dry benzene (6.4 ml) was added dropwise BF_3-etherate (0.13 ml), and the total solution was kept stirring under argon atmosphere for 2 min and neutralized with 5% aq. $NaHCO_3$. The benzene layer was washed with water and worked up in the usual manner to give an oily product (128 mg). Preparative TLC (*n*-hexane–$CHCl_3$=1:1) of the product gave A-7 (**26**) (26 mg, 22%), A-10 (**30**) (13 mg, 10%), and A-11 (**31**) (57 mg, 45%). A-7 (**26**) obtained here was identified with the one obtained above from **6** by TLC (*n*-hexane–ether=1:1), IR ($CHCl_3$), GLC, and PMR. A-10 (**30**), colorless glassy, $[\alpha]_D^{22}$ −37° (*c*=0.50, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3597, 1739, 1645, 1240, 897. PMR ($CDCl_3$) δ: 0.93, 1.03 (3H each, d, *J*=6 Hz, 11-CH_3×2), 1.09 (3H, s, 10-CH_3), 2.04 (3H, s, $OCOCH_3$), 4.36 (1H, br.d, *J*=*ca.* 9 Hz, changed to a narrow triplet on D_2O addition, 6-H), 4.91, 5.14 (1H each, br.s, 14-H_2), 5.36 (1H, m, 8-H). MS *m/e* (%): 280 (M^+, 3), 108 (100). High resolution MS *m/e*: Found 280.203; Calcd. for $C_{17}H_{28}O_3$ (M^+) 280.203. A-11 (**31**), colorless glassy, $[\alpha]_D^{22}$ −44° (*c*=1.0,

$CHCl_3$). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3607, 1735, 1643. PMR ($CDCl_3$) δ: 0.90, 1.04 (3H each, d, J=6 Hz, 11-CH_3×2), 1.16 (3H, s, 10-CH_3), 1.84 (3H, d, J=1 Hz, 4-CH_3), 2.06 (3H, s, $OCOCH_3$), 4.33 (1H, br.d, J=*ca.* 8 Hz, changed to a narrow triplet on D_2O addition, 6-H), 5.32 (1H, m, 8-H), 5.39 (1H, m, 3-H). MS *m/e* (%): 280 (M^+, 5), 108 (100). High resolution MS *m/e*: Found 280.203; Calcd. for $C_{17}H_{28}O_3$ (M^+) 280.203.

Treatment of 7 with HCOOH–Acetone (1: 1)——A solution of **7** (10 mg) in freshly distilled acetone (1 ml) and 99% HCOOH (1 ml) was left standing under argon atmosphere at 36° for 18 hr, poured into ice-water, and extracted with ether. The ether extract was washed with 5% aq. $NaHCO_3$ and water, and worked up in the usual manner. The product (10 mg) thus obtained was subjected to GLC (SE-30, 1 m×3 mm, column temp. 190°) to give a result as shown in Table V.

Treatment of 7 with CF_3COOH–$CHCl_3$——A solution of **7** (8 mg) in $CHCl_3$ (0.2 ml) was treated with CF_3COOH (0.08 ml) and left standing under argon atmosphere at room temperature for 3 min. Neutralization and working up of the reaction mixture as above gave a product (8 mg), whose GLC analysis disclosed its composition as shown in Table V.

Treatment of 7 with *p*-TsOH·H_2O–Ether——A solution of **7** (8 mg) in dry ether (0.8 ml) was treated with *p*-TsOH·H_2O (8 mg) and heated under reflux under argon atmosphere for one hour. After cooling, the reaction mixture was poured into ice-water and extracted with ether. The ether extract was neutralized with 5% aq. $NaHCO_3$ and worked up in the usual manner. The product (7 mg) was subjected to GLC analysis as above and the result was as given in Table V.

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